Archives of Neurology and Psychiatry

VOLUME 36 OCTOBER 1936 NUMBER 4

ELECTRICAL ACTIVITY OF THE CAT'S BRAIN

R. W. GERARD, M.D., PH.D.

W. H. MARSHALL, PH.D.

AND

L. J. SAUL,* M.D.

CHICAGO

These experiments on the electrical activity of the brain, begun at the close of 1932, were planned in part to observe the types of potential that appear and the influence of various chemical and other conditions on them; in part to establish an "electrical atlas" relating activity to anatomic regions. The latter end was furthered by introducing the Horsley-Clarke stereotaxic apparatus into our armamentarium during work continued in the first half of 1934. At this time research had to be interrupted for over a year. Although preliminary reports (Gerard, Marshall and Saul [1]) covering our essential observations have appeared, the full description was withheld in the hope of securing a more complete set of photographic records than we had accumulated. Since much interest in this field is now evident and our atlas may aid other investigators, we now report our findings in detail. Many of our observations have been obtained independently by other workers and can simply be summarized in this paper. Others, made without accurate localization and often with no permanent record other than a sketch of the oscillographic screen and the reports of three observers as to loud-speaker responses, are given only so far as they are qualitatively important. The bulk, obtained with the stereotaxic apparatus, is summarized in relation to the appropriate histologic picture. An attempt is made in the discussion to assess the implications of these and related data as to the nature of neural function.

METHODS OF INVESTIGATION

Animals.—Experiments were performed on over fifty cats and two monkeys, and occasionally on frog, rabbit, dog or human subjects. Cats are preferable to

* Member of the Institute for Psychoanalysis.

From the Department of Physiology, the University of Chicago.

1. Gerard, R. W.; Marshall, W. H., and Saul, L. J.: Proc. Soc. Exper. Biol. & Med. **30**:1123, 1933; Am. J. Physiol. **109**:38, 1934.

dogs for work with the Horsley-Clarke instrument because of the more constant dimensions of the skull and brain, as well as the smaller hemorrhages at operation. Monkeys are advantageous in all ways (except that of expense), especially for work on the cerebellum and underlying brain stem, which in the cat are inaccessible from above without a secondary attack on the bony tentorium. This region can, however, be effectively explored in cats by a posterior approach.

With the animal under anesthesia, the skull was opened more or less widely over the left hemisphere, the dura reflected and the exposed cortex protected with cotton soaked in warm Ringer solution. In some experiments small drill holes through the calvarium permitted insertion of the electrodes. When the stereotaxic instrument was used this supported the head and electrode, the animal's body lying free (usually wrapped in cotton) on a board or in a hammock. In earlier experiments the head was held by plates, with the jaws kept clamped on a bit, and the electrode was supported on a ratchet stand. A tracheal cannula was inserted in these animals.

That the preparations remained in good condition is evidenced by our ability to repeat at the end of the experiments, occasionally over eight hours later, observations made at the start.

Anesthesia.—The serious problem of anesthesia in experiments on brain activity will be more fully considered later. We used mainly two drugs, pentobarbital sodium, of the barbiturate series, and tribromethanol in amylene hydrate, related somewhat to chloroform. These were ordinarily given intraperitoneally in minimal doses: from 90 to 100 mg. of tribromethanol per kilogram of body weight, dissolved to form a 2.5 per cent solution, or 1 cc. of a 6 per cent solution of pentobarbital sodium for each 5 pounds (2.3 Kg.) of body weight. Sometimes anesthesia was deep enough to permit the operation after from one fourth to three fourths of an hour; often ether was required during the actual dissection. Regularly, from two to three hours was allowed between the induction of anesthesia and the beginning of observations, so that any action of the ether had passed and even the basal anesthesia was considerably diminished. Commonly, animals were lightly enough anesthetized so that winking and movements of the pinna occurred spontaneously or on gentle stimulation of the body. Fortunately, little if any pain is involved in exploring the brain with a needle electrode, so that even very lightly anesthetized animals ordinarily remained quiet during an experiment. Occasionally an additional whiff of ether or a further injection of the drug was needed, especially in protracted observations. The depth of anesthesia was deliberately increased in a number of experiments, as will be reported.

Localization.—A crude localization can be obtained from surface relations and the depth of penetration of the needle, but histologic control is required for finer definition. With sometimes as many as one hundred points explored electrically in a single brain, such anatomic analysis, if not impossible, would require extensive facilities far beyond our means. Fortunately, needles can be placed rather accurately with the aid of the Horsley-Clarke stereotaxic instrument, and we have relied on its three dimensional coordinates for our localization.

A needle tip can be placed with this instrument certainly within an error of 0.5 mm. in a given brain. From one animal to another, however, greater latitude is possible, owing to differences in the height of the calvarium and exact relations of the auditory canals, slight herniation of the brain toward the open side, etc. We cannot insist, therefore, on an accuracy closer than 1 or 2 mm. in defining particular tracts and nuclei as the locus of observed activity. In the great majority of instances, involving several thousand point observations, results for different animals agreed well with one another, and the type of activity found was in harmony with the present views as to the function of the neurologic region

where it was located. We believe, therefore, that the Horsley-Clarke coordinates in our series can be translated with considerable confidence into regions of the brain even in the absence of direct histologic control. This will, of course, be necessary for a finer study of particular nuclei or other units, but the following data are reported as a first approximation to a delineation of local electrical activity throughout the brain. In a few instances our findings are at variance with accepted views derived from anatomic study. When our experiments were often repeated it would seem that errors in localization were excluded, but when only one observation was made the localization to a small structure by Horsley-Clarke coordinates alone is not to be taken as established.

The use of the Horsley-Clarke apparatus has been adequately described by its creators (Horsley and Clarke,[2] and Clarke and Henderson[3] and, after an unaccountable period of desuetude, by Ranson and his colleagues (Ingram, Ranson and others[4]). Dr. Ranson gave assistance in the use of the instrument[5] and, especially, made available to us serial sections of the cat's brain cut coronally in the plane of the Horsley-Clarke machine. These were used for preparing enlarged photomicrographs with coordinate lines superposed, some of which are reproduced in this paper. Dr. S. Polyak has given us invaluable assistance with the morphologic aspects of this work.

The degree to which the recorded potentials are localized at the electrode tip is better considered in relation to the electrode.

Electrodes.—Except for a few comparative tests, all observations were made with the concentric needle electrode introduced by Adrian and Bronk.[6] A fine insulated copper or silver wire, (copper was entirely satisfactory) was fixed in a 3 inch (7.6 cm.) hypodermic needle, ground at its tip to a level plane and beveled so that the wire formed the apex of a cone. Needles of from 20 to 24 gage were used, and the wire was allowed to protrude from 0.25 to 1 mm. The wire was connected to the grid and the needle shank to the ground through shielded wires and connections. Sometimes an extra ground lead as well was taken from under the skin of the neck, especially for observations on the cortical surface.

Such a concentric electrode was chosen because it permits extremely exact localization. That this is so was demonstrated amply by the present findings. Responses often change abruptly on moving the electrode 0.5 mm., so that strong electrical activity vanishes. In extreme cases we observed successively, within an area of movement of 1 mm.: no response to auditory or optic stimulation, strong response to optic stimulation, no response, strong response to auditory stimulation and no response. Clearly, only local potential differences between the grid and the surrounding ground lead were recorded. Electrocardiograms and muscular movements did not appear, although sometimes a twitch of the ear came through.

The penalty for such localization is diminished sensitivity, especially to slow and widespread electrical changes carrying grid and ground together on the same

2. Horsley, V., and Clarke, R. H.: Brain **31**:45, 1908.

3. Clarke, R. H., and Henderson, E. E.: J. f. Psychol. u. Neurol. **21**:391, 1911.

4. Ingram, W. R.; Ranson, S. W.; Hannett, F. I.; Zeiss, F. R., and Terwilliger, E. H.: Results of Stimulation of the Tegmentum with the Horsley-Clarke Stereotaxic Apparatus, Arch. Neurol. & Psychiat. **28**:513 (Sept.) 1932.

5. Mr. R. Kittel, of the department of chemistry of the University of Chicago, constructed a slightly modified and satisfactory instrument for us, and since then for a dozen others. The price is $150, without special accessories.

6. Adrian, E. D., and Bronk, D. W.: J. Physiol. **67**:119, 1929.

potential wave. The largest potentials were 100 or 200 microvolts (in one instance auditory potentials up to 500 microvolts appeared), and the smallest, at the noise level of the amplifier, 2 or 3 microvolts. The extent to which large, slow waves were missed will be considered later, but at least waves lasting over a second were recorded. Also, continued rapid waves, not noted by investigators using diffuse electrodes, are often clearly seen with the localized type.

Polarizable metal electrodes are capable of introducing serious errors when microvolt potentials are in question. The dangers of microphonic and coarser mechanical pick-up are recognized, although surprisingly large potentials may be generated under certain conditions by tapping an insulated surface at a distance with the finger-tip. Less apparent attention has been directed to electrolysis and battery action, especially when different metals form the two leads. An input condenser and a low external input resistance (as with the concentric electrode) greatly diminish disturbances of this sort. Evaporation from or condensation on an exposed electrode or its close vicinity can evoke an array of potential discharges that amazingly simulate biologic activity. Spikes and sine waves, regular and irregular, of low and high frequency and stopped by ether or by cooling, obtained from the forebrain of an embryonic chick, almost convinced one of us that they were genuine discharges, though they were really due to condensation of water on a platinum electrode. Finally, in almost any metal in contact with a saline solution potentials develop when light is flashed on or off—up to several millivolts in the case of silver (see also Audubert [7] and Fry and Bartley [8]).

The potentials obtained were but little confused by stimulation or injury due to the insertion of the electrode. During actual movement changes in potential developed, owing in large part to mechanical factors, but with the needle in position responses were usually constant and reproducible. In the hypothalamus pupillary changes and the like indicated stimulation by needle movements. Since, further, observations made during the first penetration could be repeated during withdrawal of the needle or during subsequent reinsertion in its track, no serious damage could have been done to the tissue. Occasionally responses that were strong just after placing the electrode faded gradually in one or two minutes—whether owing to initial stimulation or injury or to physiologic variation is not certain. The predominance of intense, high frequency discharges of short duration from certain regions, mainly in the ventral portion of the brain stem, indicates, however, an important cellular factor. The rigid attachment of the electrode to the skull prevented pick-up from ordinary movements or vibration, but pulsations of the brain with the heart beat and with respiration may cause rhythmic potentials that must be carefully distinguished from genuine activity.

Recording System.—A three-stage, resistance-capacity-coupled amplifier and high voltage oscillograph, as previously described (Gerard and Marshall [9]), and a loud-speaker were used. Records of a single trace were obtained by contact prints or, mainly, with an ordinary camera supplied with a portrait lens and a verichrome film pack. A nearly linear time axis, obtained by discharging a condenser through a diode tube, was checked by the use of 60 or 2,000 cycle sine waves. Sensitivity and distortion were determined with rectangular waves from a commutator passed through a potential divider. A potential of 2 microvolts at the input was visible above the base line, and square waves of as much as a twentieth of a

7. Audubert, R.: Phénomènes photoélectrochemique, Actualités scien. et indust. 1934, vol. 91.

8. Fry, G. A., and Bartley, S. H.: J. Cell. & Comp. Physiol. **5**:291, 1934.

9. Gerard, R. W., and Marshall, W. H.: Am. J. Physiol. **104**:575, 1933.

second showed no distinct distortions. (Some of the records reproduced in this paper were obtained later with a continuous film camera.) More recently a high speed ink writer has yielded excellent records.[9a]

For much of the work, emphasis was laid on what could be heard from the loud-speaker, despite the lack of permanent record. Three observers regularly agreed in judgments, even of a semiquantitative nature, and many phenomena, hardly to be detected in the oscillographic trace or in the photograph of one sweep, were clear to the ear because of its ability to integrate in time. This was especially striking for spontaneous or "background," activity, which sometimes showed for a small needle movement a distinct, sharp change in character as heard over the speaker, with no obvious change in the trace. Oscillographic changes can, of course, be analyzed from a continuous record, but without a clue from the ear the eye would often miss them. A low pass filter in the output is often useful in emphasizing regular, slow changes.

Stimulation.—Ordinarily, crude stimulation was used: Light was flashed into one or both eyes, or an object was moved before them (sometimes the pupils were dilated with atropine, and the nictitating membrane was retracted); sound stimuli were produced by a metronome, forks, the voice and metallic clicks, such as the tick of a watch; touch was elicited by cotton or a glass rod, the latter of which also served to produce pressure and move joints; and ammonia vapor, alcohol and asafetida served for smell. For more exact study of the latent period and the amplitude of response a stimulus was delivered by means of a thyratron, which also controlled the sweep circuit of the cathode ray tube. For light the practically instantaneous flash of a neon lamp was used. For sound the click of a telegraph key and for pressure or proprioception the movement of the key arm, attached by wire or thread to the toes or leg, was utilized. The thyratron discharge showed as a small artefact in the trace, so that latent periods were easily determined. Other than rough quantitative and qualitative variations, no systematic study of the range of stimuli was made.

RESULTS OF INVESTIGATION

Our results can best be presented in two portions: a description of observed phenomena and a tabular summary of the anatomic coordinates at which they appeared. In the text, a tentative assignment of an electrical activity to a particular structure will often be made, on the basis of its coordinates. The atlas is composed of photomicrographs of ten coronal sections of the cat's brain, representing planes on the anteroposterior axis of the Horsley-Clarke apparatus, at from 2 to 3 mm. intervals, from 16 mm. anterior to 4 mm. posterior to the interaural zero plane. Distances lateral (to the left in all instances) from the midsagittal plane and above or below (+ or —) the zero horizontal plane (heavy line) of the instrument are indicated on each plate by the coordinate lines. In the enlargements as used, a distance of 1 mm. in the brain is 1.0 cm. on the photograph, represented by the coordinate lines. In the reproductions also a small square represents 1 sq. mm. For each point, therefore, there are an anteroposterior (A-P) coordinate, which is given by the plate as a whole, and left-right (L-R) and (+ and —) coordinates, which are read from the plate.

9a. Offner, F., and Gerard, R. W.: Science **84**:209, 1936.

Opposite each photomicrograph are listed electrical activities observed in the neighborhood of its anteroposterior plane with localization by their other coordinates, and for the reader's convenience some of the major anatomic structures are also indicated in terms of their coordinates.

A needle placed almost anywhere in the brain, as well as on its surface, records more or less electrical activity. Since these potentials are present in the absence of deliberate stimulation, we have called them spontaneous, background or resting potentials. It is, of course, impossible to exclude sensory and reflex activities, and, in fact, these spontaneous potentials are most striking in the definitive sensory and motor systems and in some reflex centers, for example, the cardiac centers. In many ways, however, they are distinct from the activity evoked by deliberate stimulation, so that it is useful to consider separately the spontaneous and the evoked activities of the brain. Only in the case of the optic system is it simpler to consider the two together. It should be emphasized that in each experiment various types of stimuli were tested at each position of the electrode. Only where distinct potentials were evoked are results mentioned. Auditory potentials, for example, did not appear in the optic tracts, though they were tested for there, as elsewhere.

Evoked Potentials.—Potentials from Auditory Structures.—Electrical activity definitely evoked by sound stimuli was obtained from: the accessory acoustic nucleus; the trapezoid body; the lateral lemniscus; the superior olive; the brachium conjunctivum; the inferior colliculus, especially the nucleus of the colliculus; the medial geniculate body; the corona radiata; the cortical gray matter, in some instances the surface, of the median and posterior ectosylvian and suprasylvian gyri, and in two instances, the posterior splenial gyrus. In three instances activity was recorded in the anterior part of the cerebellum. In one case auditory responses were obtained in the striate area, near the lateral margin of the lateral gyrus. Most of these structures are part of the recognized auditory system. Relatively few auditory points were studied with the Horsley-Clarke apparatus in place because of the inevitable damage to the middle ear, and most observations other than those of localization were obtained without precise coordinates.

The threshold was low for evoked potentials in the important auditory paths. A distant watch tick or whisper, barely audible to an observer near the cat, produced clear responses of the oscillograph or speaker, with an electrode, for example, in the geniculate body. In the colliculus occasionally potentials up to 0.5 millivolt, the largest we obtained, accompanied the tick of a watch hung 5 cm. from the ear. It follows that activity is not uniform throughout these structures, else the concentric electrode would record nothing, and it was, in fact, possi-

ble to demonstrate sound localization. Thus, with the needle in one position responses to the tick of a watch were much more marked than those to the voice (humming a given tune), while with the needle placed 2 mm. caudad the voice carried a strong response and the tick a weaker one. More rigorously, standing waves on the synchronized oscillograph were obtained for different pitches at different positions of the electrode. In an experiment on a monkey, with the electrode leading probably from the corona radiata, an almost perfect sine wave of correct frequency was obtained on sounding the fork giving 660 double vibrations, while words appeared as irregular bursts. Moving the needle slightly laterally left the word response not visibly different but eliminated the sine wave. From the inferior colliculus of the cat, on the other hand, standing waves appeared with the fork of 660 double vibrations or with the voice; as the pitch of the voice was progressively raised or lowered the waves appropriately increased or decreased in frequency.

The shape of the wave in the response to a constant and fairly simple sound—watch tick, metronome beat or click of a forceps—is constant for a given recording position, but far from simple. The spread of cochlear potentials did not confuse these observations of strictly neural activity (Saul and Davis [10]). Some characteristic shapes are indicated in figure 1, and it need hardly be emphasized that at present any attempt to interpret them in detail in terms of structure or function would be highly gratuitous. Certainly, the particular structures that are active influence the contour, for this may differ widely at one point when a watch is held to the right and when it is held to the left ear. Only different patterns about the electrode of neurons actively carrying impulses from the crossed and uncrossed cochleae, respectively, could produce such variations. The same point is brought out when the needle is moved slightly, remaining, however, in the same anatomic unit, a continuous change in potential shape being noted in response to a fixed stimulus. The response can be greatly modified still further, even with a constant stimulus and lead, by changing the state of the brain, as, for example, by inhalation of carbon dioxide. All these points are illustrated by sketches from the tube face (fig. 1).

Since the entire form of the response can be profoundly varied by all these factors, much additional information is needed to enrich with meaning individual waves and spikes. It is worth noting, however, that the triple spike response is fairly often encountered; especially since Davis and Derbyshire [11] observed a similar triple response in the

10. Saul, L. J., and Davis, H.: Action Currents in the Central Nervous System: I. Action Currents of the Auditory Tracts, Arch. Neurol. & Psychiat. **28**:1104 (Nov.) 1932.

11. Davis, H., and Derbyshire, A. J.: Am. J. Physiol. **113**:476, 1935.

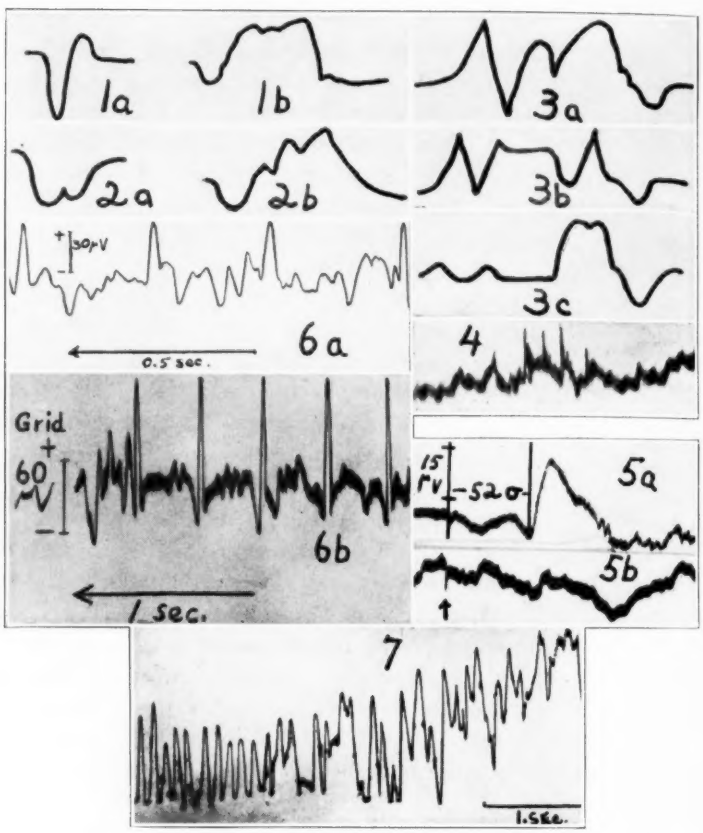

Fig. 1.—Tracings showing auditory responses. *1*, *2* and *3* are semidiagrammatic sketches made from the tube face, with the electrode in the auditory thalamus. *1* shows the response to the watch tick heard (*a*) with the right ear and (*b*) with the left ear, at the same position of the electrode; *2*, the response to the watch tick heard (*a*) with the right ear and (*b*) with the same ear, with the electrode 1 mm. deeper, and *3*, the response to the watch tick (*a*) before inhalation of carbon dioxide, (*b*) seven minutes after starting inhalation of carbon dioxide and oxygen (respiration had stopped, and artificial respiration was employed) and (*c*) after nine minutes' inhalation of carbon dioxide and oxygen. *4* shows the response to the watch tick heard with the right ear, with the electrode in the nucleus of the inferior colliculus (AO L4 —1); *5*, the response to the telegraph key, with the electrode in the inferior colliculus (AO L4 + 2), *a* indicating an artefact from the thyratron and the response to the click and *b*, the same, but with the click deadened as a control; *6*, the response to the metronome beat at 3 a second, with the electrode in the nucleus of the inferior colliculus (lateral lemniscus) (A2 L6 —1), *a* being taken with a fast film and low pass filter and *b*, with a low film and no filter; and *7*, the response to the watch tick from the auditory cortex (A12 L12 + 10), showing double spikes.

auditory nerve. It is probably true, and even more clear in the case of the optic system, that the more neurons there are in the path from receptor to recording point the more complex the potential is likely to be. This would be consistent with a grouping and reorganization of nerve impulses each time that they were relayed from one fiber bundle to another. Large numbers of tract fibers are also probably activated by small numbers of afferent fibers (to be discussed later). Auditory potentials in the thalamus of the rabbit were less complex than in that of the cat.

It is perhaps surprising that, after such "neural work" in reintegrating the trains of relatively raw impulses reaching the central nervous system, many of the original characteristics persist. Even when picking up potentials from the thalamic nuclei and, probably, the corona radiata, responses of the loud-speaker resemble the original sound stimuli. The watch tick or metronome beat is easily recognized over the speaker, and the ticks of different watches can be identified even though the quality is altered; songs presented to the cat's ear can often be recognized over the speaker, although the words are lost unless divined from the melody, which remains clear.

An especially interesting observation was made on at least five cats when the needle happened to engage both the auditory and the optic tracts, as between the geniculate bodies. The response to a given auditory stimulus is increased during the time a light is thrown on the eyes. This facilitation or interaction may be sufficient to render audible from the speaker a watch tick too feeble to be detected in its absence. The increased response is not due to an inflow of optic impulses into auditory paths, for the characteristics of each type of response are retained. Further, in one instance, there was a clear lag of from two to five seconds between turning on or off the light and the increase or decrease of the auditory response, although the optic response was prompt. In this experiment also the auditory response was increased only by light in the eye of the same side (that contralateral to the electrode), although optic responses were obtained from both eyes; in another instance only the opposite (ipsilateral) eye had such an effect. The possible significance of this phenomenon will be considered later; it is important now to note that activity in one set of paths may affect that in another, without nerve impulses being actually conducted across.

Potentials from Somesthetic Structures.—Impulses from the head, trunk and limbs were traced through many structures. In the midbrain they appeared in the medial lemniscus; the reticular formation; the dorsal portion of the superior olive; the spinal fifth root; the nucleus of the inferior colliculus; the brachium pontis, and in one instance, the cerebellum. A wide representation in the thalamus includes: the ventral thalamic nucleii; the dorsal and ventral parts of

the large lateral nucleus; a strong representation in the ventrolateral nuclei and the reticular substance lateral to it; and occasional findings in the hypothalamic region, such as the H_2 fibers between the ventrolateral portion of the thalamus and the subthalamic body of Luys and the area near the fasciculus retroflexus of Meynert.

Above the thalamus impulses appeared in: the reticular substance ventrolateral to the globus pallidus; the internal capsule and corona radiata, especially lateral to the dorsal portion of the lateral nucleus, and through the depth of the radiations lateral to the head of the caudate nucleus and, possibly, in the head of the caudate nucleus itself. In or on the cortical gray matter, activity was most marked in the middle and anterior portions of the suprasylvian gyrus and the middle ectosylvian gyrus, but it appeared as well in deep portions of the anterior sylvian gyrus, the anterior ectosylvian gyrus, the lateral gyrus and the suprasplenial gyrus dorsal to the deep splenial sulcus. More anterior regions, including the coronal and sigmoid gyri, were not explored systematically, but activity was strong and localized in the posterior sigmoid gyrus.

Responses were predominantly but not exclusively crossed, and the responses from the forepaw overshadowed those of other sensory fields. It is often impossible to be certain of the stimulus modality that is involved in these responses. When light touch to hairs evokes activity this can reasonably be ascribed to tactile receptors. When potentials appear on squeezing, after touch has been found ineffective, these are considered to arise from pressure stimuli. When movements of the toes, foot, etc., give responses fairly proportionate to the movement, while pressure is maintained roughly constant, these impulses are considered to be proprioceptive.

Since pressure and touch relations cannot be kept uniform with movement (e. g., hairs rub against one another) nor can slight movement be excluded during pressure, such separation of sense qualities is only approximate. Real differences exist, however, in the type and location of responses to these different stimuli, for when the needle is moved 1 or 2 mm. in the lateral thalamic nucleus, a response may be given in one instance only to touching a toe, and in the other, only to bending it.

Various regions yielded responses to local receptor fields—a single paw, leg, shoulder or jaw or the various regions of the trunk. Impulses from the forefeet and hindfeet were obtained in separate portions of the medial lemniscus. In the lateral thalamic nucleus proprioceptive impulses were dorsal to tactile and were strongest more rostrally as well. Proprioceptive discharges on opening the jaw appeared in the internal capsule, near the globus pallidus. The shoulder was represented in

the suprasylvian gyrus in one instance. In two monkeys tactile responses were strong from the surface of the postcentral gyrus, and proprioceptive responses, from both the precentral and the postcentral gyrus, and the arm, leg and other regions were localized at the same level as that of the corresponding motor points of the precentral gyrus. In most experiments on cats the crossed forepaw was most widely represented; i. e., impulses from this region were found in nearly all the somesthetic regions. On the whole, the crossed responses were more pronounced than the uncrossed, those for the foreleg more marked than those for the hindleg and those for the paw more than those for the leg.

Greatest responses were obtained from the ventrolateral thalamic nuclei; unmistakable activity resulted from touching a single hair of the forepaw with a hair on the observer's hand so lightly that the observer felt nothing. With the arm of a telegraph key tied to a toe, responses were obtained with the thread so slack that one could not feel any jerk or vibration when holding it with the finger-tip, although this holding sufficed to stop the mechanical stimulation of the paw and the brain potentials.

The period of latency varied from 12 milliseconds with strong stimuli to 17 milliseconds with threshold stimuli. These values are only approximate, since some time must have elapsed between the electric pulse to the key and the mechanical pull to the foot, especially with a slack thread, but the error cannot be one of many milliseconds.

It is striking that responses to stimulation of one receptor can be picked up in a mass of brain tissue with a concentric electrode. Inactive regions always shunt the input, and it is not possible to record impulses in one or a few fibers under these conditions. Even in the isolated spinal cord of the frog of the Baglioni preparation, impulses ascending in the lemniscus from extensive cutaneous stimulation of the leg are barely detectable with a concentric electrode, athough they are clear with separated leads (Gerard and Young [12]). In the frog cord the mass of active fibers is great in relation to the cross-section of the tissue although small absolutely as compared with tracts in the neuraxis of the cat. Since only inactive tissue shunted between the leads is important, which is a very limited region with use of the concentric electrode, the actual rather than the relative mass of active elements is the more critical. In other words, the number of active units in the immediate vicinity of the electrode rather than the number in relation to the total mass of tissue determines the magnitude of the potentials obtained, and with our system activity in a considerable number of elements is required to give clear responses. It follows that by the time the thalamus is reached impulses originating even in a single receptor have engaged many parallel neurons conducting

12. Gerard, R. W., and Young, J. E., to be published.

centripetally. This is further evidenced by changes in the length of latency with various stimulus strengths and by changes in potential pattern at successive levels of the pathways.

Potentials, even in fiber bundles, may be rather long, single waves and often flat topped, rather than a series of brief polyphasic waves. Figure 2 shows typical responses from the ventrolateral thalamic nucleus and tracts.

Spontaneous activity of the somesthetic paths is rather marked, and in general the stronger the background potentials the greater the

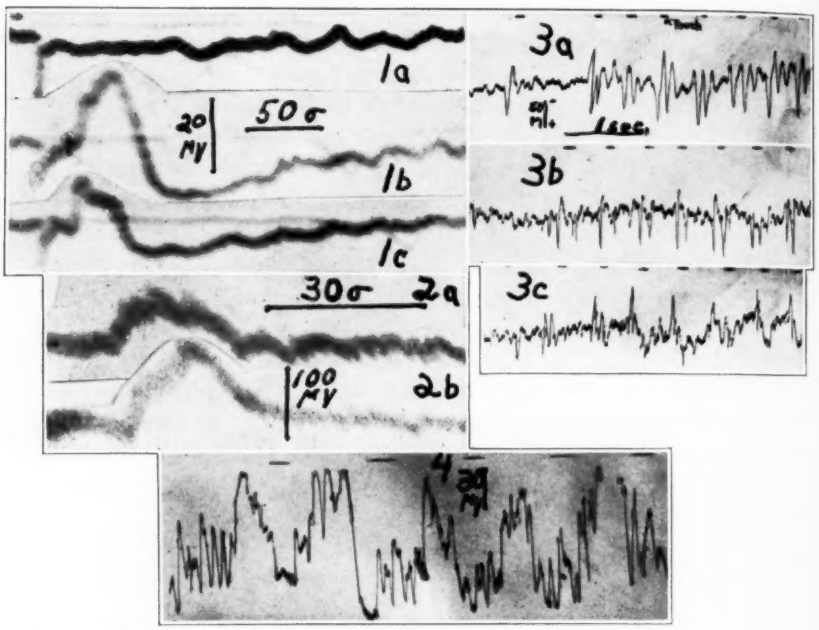

Fig. 2.—Tracings of somesthetic responses. *1* shows the response from stimulation of the right hindpaw by a thyratron-controlled telegraph key, with the electrode in the ventrolateral thalamic nucleus (A8 L6.5 0); *a* indicating a stimulus artefact obtained as a control, with a loose thread clamped between the fingers, *b*, the results of stimulation of the same paw with the string taut and *c*, the response with the thread loose so that only vibration reached the paw; *2*, the response when the paw was moved by the thyratron, with the stimulus at the start of the trace, the electrode being placed below the ventral part of the lateral thalamic nucleus (A10 L5 — 1), *a* indicating the response to a strong pull and *b*, the response to a weak pull, with a longer period of latency; *3*, responses to the touch of a forepaw, indicated by a signal, with the electrode in (*a*) the basal cerebellar nuclei (P8.5 R2 + 2) (uncrossed forepaw), (*b*) the medial lemniscus (P8.5 R2 10) (uncrossed forepaw) and (*c*) the same area as that indicated in *b*, but for the crossed forepaw; and *4*, response to several touches of the crossed forepaw, indicated by the signal, with the electrode in the somesthetic cortex (A16 L10 + 10).

response on peripheral stimulation. The ventrolateral thalamic nucleus was especially active in cats, and the postcentral gyrus, in monkeys. The response may be a brief burst, with little after-discharge, or for more prolonged stimuli (a squeeze or stretch) it may show clearcut "on" or "off" effects or both, or any of these combined with a discharge continuing through the period of stimulation. In one instance, on either flexing or extending the toes, the response appeared only at the end of the movement, and in another a large, slow wave followed at a definite interval after squeezing the abdomen—possibly part of a late reflex response. Not infrequently, successive volleys of impulses occurred with no deliberate stimulation, although they were increased by it. Sustained volleys in the corona radiata resulted from loosely enclosing a paw, and in one instance roughing the hair of the back gave volleys every twenty seconds until it was again smoothed down.

Some rhythmic discharges were present in cutaneous paths and were modified by cutaneous stimulation. Thus, in the lateral thalamic nucleus activity lasting three seconds recurred every ten seconds, and regular rhythms, changed by cutaneous stimulation, were observed in the medial lemniscus, the nucleus of the inferior colliculus, the reticular formation of the midbrain (at 2.3 a second) and the suprasylvian gyrus. These are particular examples of other rhythms to be considered later.

Potentials from Optic Structures.—Flashing light in the eyes led to potentials in the optic nerves and chiasm and the tracts passing caudally from it. Potentials appeared also in: the lateral geniculate body; the dorsal thalamic nucleus; the lateral thalamic nucleus; the superior colliculus; the inferior colliculus and its commissure, and, occasionally, in the descending limb of the fornix or the adjacent hypothalamic structures and the hypothalamic commissure. Activity was further noted: in the internal capsule; possibly in the near-by tail of the caudate nucleus; widely in the radiations; and in the cornu ammonis and the amygdala; as well as in and on the gray matter of the cerebral gyri and sulci, including the lateral, posterior lateral, suprasylvian, posterior suprasylvian, posterior ectosylvian, suprasplenial, posterior splenial, fornicate and pyriform gyri. Optic activity was also traced into the cerebellum. Responses were especially strong in: the primary optic tract, the lateral geniculate body, the cornu ammonis and pyriform lobe, the radiations to the posterior lateral and fornicate gyri, the gray matter at the base of the suprasylvian fissure and the posterior suprasylvian gyrus. Though the cornu ammonis is not considered to be optic in function, we have thirteen separate observations of optic responses located in this structure. It is hard to believe that in each instance an error of placement into or

electrical spread from near-by optic structures was responsible, although the possibility has not been excluded.[13]

In the cat activity was recorded from the cortical surface over the whole striate area, as defined by Poljak's[14] experiments on degeneration, rather than over the more restricted cyto-architectural area (fig. 3). Responses increased in intensity with penetration to about 3 mm. and then decreased in general to a minimum at from a depth of 7 to 10 mm. In the monkey, the maximum response was at a depth of 7 mm. These figures are approximate, since the folding of the gray matter gives varying relations, but it seems that the deep gray matter or the junction of the gray and white matter is the region from which the greatest cortical potentials are obtained. (The work of Dusser de Barenne and McCulloch [15] on cortical potentials after thermocoagulation may be relevant to this point.)

Responses from the contralateral eye ordinarily predominate over those from the ipsilateral eye in the optic paths and cortex, but many exceptions exist. Several points on the cortical surface responded equally to light in either eye, and others, to light in the contralateral eye only. Bilateral equality was more developed in the monkey than in the cat paralleling the greater development of binocular vision. Varying relations from equality of response to crossed predominance were noted in different regions of the radiations, and in the cornu and the primary tracts positions were observed in which needle movements of less than

13. Over thirteen points in six cats, located well within the cornu ammonis, according to the Horsley-Clarke coordinates, gave strong optic responses and often optic rhythms. In view of the heterodoxy of attributing optic activity to this structure, however, a special experiment was made as a control. The needle was inserted at A2, L8 to a depth of + 3.5 mm., with the usual observations of activity, and the brain was then perfused in situ with a solution of formaldehyde. Subsequent anatomic examination showed the needle track exactly in the correct position (chart for figure 13). Optic responses were present above the position + 8 (optic radiations), showed a slight change in character below the position + 8 (top of the cornu ammonis) and a marked change at the position + 6 (center of the cornu) and disappeared at the position + 4 (bottom of the cornu ammonis). Since the optic tract, the geniculate body and the rediations are anterior, superior or lateral to the cornu ammonis, the position in the ventromedial aspect and near the posterior margin of this structure minimizes the possibility of the electric spread. Furthermore, the change in the character of response in the center of the cornu ammonis speaks against a diffuse pick-up, as does other evidence previously indicated. Spread from the optic radiations along the grounded shank of the needle, which passes through them, is also excluded, for if it were present responses would not disappear sharply when the needle tip is advanced from the position + 4 to the position + 3.5 after spreading from + 8 to + 4. Tactile responses from the contralateral nares were also obtained in the cornu.

14. Poljak, S.: J. Comp. Neurol. **44**:197, 1927.

15. Dusser de Barenne, J. G., and McCulloch, W. S.: Am. J. Physiol. **114**: 692, 1936.

1 mm. changed the response from a strictly contralateral one to one approaching (although never reaching) bilateral equality. Aside from the particular magnitude and form (to be discussed later) of the direct optic response from stimulation of one or the other eye, the two eyes often produced strikingly different effects on the optic rhythms and background, which will be considered later.

The threshold for clearcut optic responses was low. Opening and closing a forceps or slightly moving a finger illuminated only by diffuse room light and held 1 or 2 feet (30 or 60 cm.) from the eyes gave definite responses in the chiasm, optic tract, lateral geniculate body or

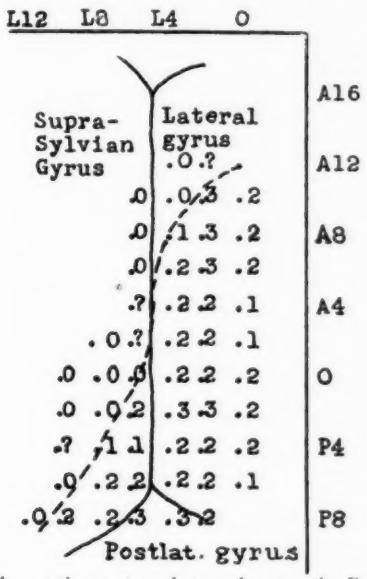

Fig. 3.—Plot of the optic cortex from above. *A*, *P* and *L* give Horsley-Clarke coordinates. Responses obtained from a concentric electrode resting on but not penetrating the cortical surface are indicated as follows: *O* signifies absence of responses; *?*, a doubtful response; *1*, presence of a weak response; *2*, presence of a moderate response, and *3*, presence of a strong response. The surface was explored in steps of 2 mm., or less.

posterior suprasylvian gyrus of various cats, and in the crossed optic lobe in two frogs. Dark adaptation increased the response to this stimulus as well as to more intense stimuli.

No systematic study of latency has been made, so that the following data are only semiquantitative. The shortest interval obtained from flash to response, twenty-five milliseconds, was with the electrode in the lateral thalamic nucleus. (No data were obtained for the primary tracts.) A latency of fifty-two milliseconds was noted in the inferior colliculus, followed by a wave lasting fifty-one milliseconds (compare

these values with those of Wang [16]). In the lateral geniculate body responses appeared after a delay of from one hundred and one to one hundred and twenty-three milliseconds when light was turned on, and a delay of only twenty-four milliseconds when the light was turned off. A diphasic or triphasic wave following the turning on lasted two hundred and fifty milliseconds or longer. The period of latency was shortest when both eyes were illuminated (one hundred and one milliseconds in two tests), longer with the ipsilateral eye alone (one hundred and six and one hundred and five milliseconds) and distinctly longer with only the contralateral eye (one hundred and twenty-three milliseconds in two tests, fig. 4). Stronger intensity also decreased the period of latency, although this was not explored. This has been more fully studied by Bartley.[17]

The character of the response was highly variable with the position of the electrode and, to a lesser extent, with the stimulus. Clear bursts with both "on" and "off" stimuli were generally obtained, but sometimes with only one, and often the response was maintained evenly during illumination, with or without an additional burst at one or both ends. The off response ranged from a burst lasting a fraction of a second to intense, maintained after-discharges, which gradually faded to the original background level of intensity during a period of two minutes or more. Such prolonged after-activity was observed in the pyriform cortex and the optic tract and adjacent hypothalamic region, and somewhat less in the lateral geniculate radiations and occipital cortex. (Hartline [18] has observed similar continued discharges from the darkened frog retina.) Small shifts in needle position sometimes altered even these gross characters of the activity. In one of two positions in the cornu ammonis 0.5 mm. apart, for example, sharp, strong responses were shown both at on and off stimulation, and in the other, at on stimulation only. Another pair of points, 1 mm. apart, more ventral in the cornu, alike gave waves of high frequency, strong and maintained on potentials, but the off response in one instance was a sharp burst, while in the other it was maintained for half a minute. The continuous discharges during or after illumination differed widely in character, from fine, rapid oscillations of high frequency to large, coarse, oscillations of low frequency in irregular or semiregular sequence. This character is determined by position, since it was not altered by stimulating either eye alone but did change, often suddenly, with a gradual shift of the electrode.

16. Wang, G. H.: Chinese J. Physiol. **8**:121, 1934.
17. Bartley, S. H.: Am. J. Physiol. **110**:666, 1935.
18. Hartline, H. K.: Am. J. Physiol. **113**:59, 1935.

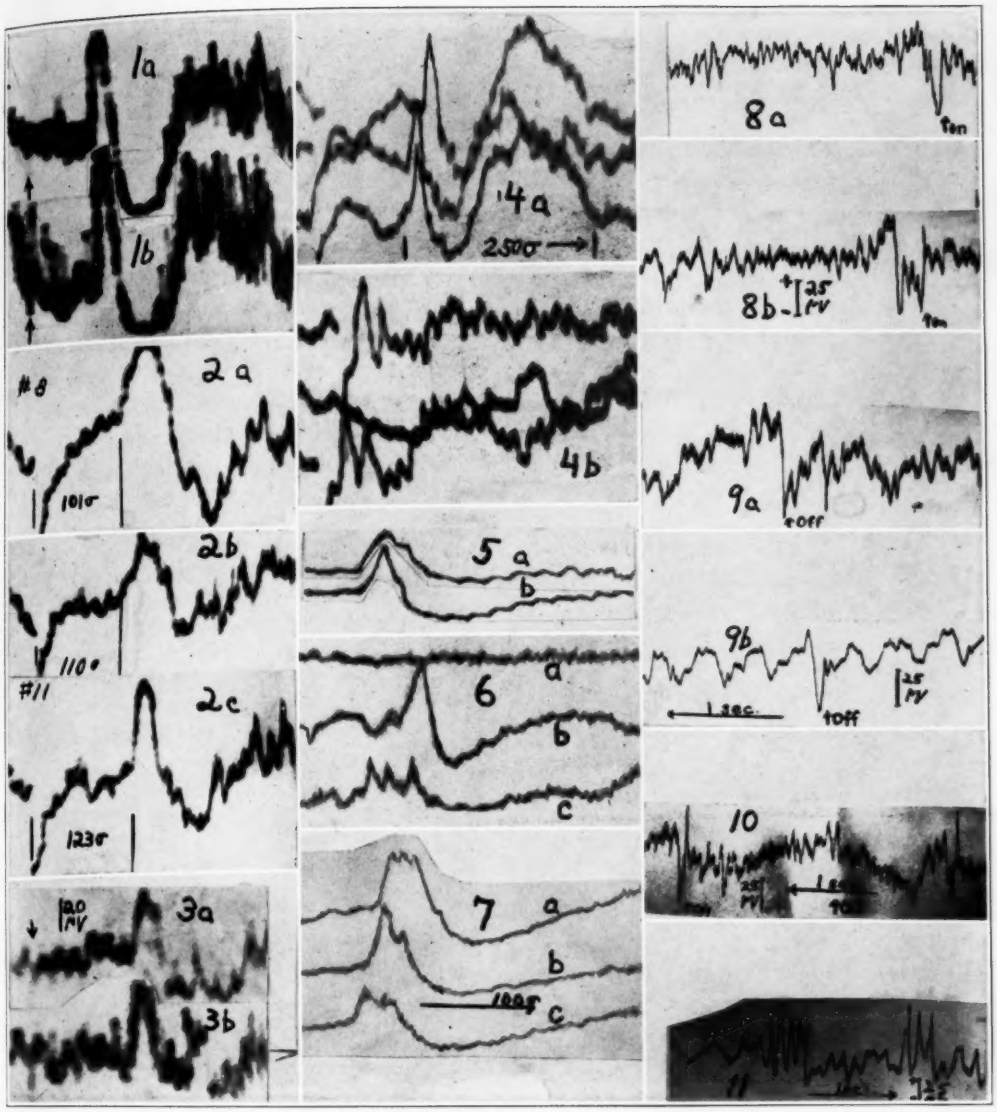

Fig. 4.—Tracings showing optic responses (periods of latency). *1 a* and *b* show two on responses of the cornu ammonis (A8 L8 — 4.5) (note the increased activity at the end); *2*, periods of latency of the on responses of the optic tract (A8 L8 + 1.5), with stimulation of (*a*) both eyes, (*b*) the ipsilateral eye and (*c*) the contralateral eye; *3 a* and *b*, two responses of the optic tract (A8 L8 + 2) to the movement of the finger in room light, held *2* feet in front of the eyes; *4*, responses to stimulation of both eyes in the inferior nucleus of the lateral geniculate body (A8 L8 + 3.5), showing (*a*) three on responses and (*b*) two off responses and a control, with a much briefer period of latency than that for the on responses; *5*, an on response of the optic tract (A12 L5 —2) to stimulation of (*a*) the right eye and (*b*) the left eye; *6* (*a*) record from the lateral geniculate body (A8 L8 + 5) with no light stimulus (control), (*b*) an on response to a dark-adapted eye and (*c*) an on response after illumination of the eye for two minutes; *7*, on responses of the optic cortex (A4 L3 + 15), with stimulation of (*a*) both eyes, (*b*) the left eye and (*c*) the right eye; *8*, on responses with stimulation of both eyes of (*a*) the lateral geniculate body (A8 L8 + 4.5) and (*b*) the lateral geniculate body (A8 L8 + 5.5), showing forms of successive responses at positions 1 mm. apart, the time axis being the same as that for the responses shown in *9*; *9*, off responses to stimulation of both eyes of (*a*) the lateral geniculate body (A8 L8 + 5.5) and (*b*) the beginning optic radiations (A8 L8 + 6), showing a comparison of the forms; *10*, on, off and on responses of the lateral geniculate body (A8 L8 + 3.8); and *11*, on and off responses of the optic cortex (P4 L7 + 15).

The main waves associated with turning light on or off, however, depend on the eye excited and the type of stimulus, as well as on the region of the brain. Various types are illustrated in figure 5. It will be noted that at a given electrode position the on and off waves differ, as do those from stimulation of the right and the left eye and both eyes, and on shifting the position the entire profile may be changed. Single monophasic sinelike potentials, a monophasic "spike" followed by a prolonged hump, two humps in one direction, a diphasic spike and single hump, diphasic and polyphasic humps, etc., were all seen. From a lead in the pyriform cortex the on and off bursts were perceptibly delayed after the stimulus (estimated at two seconds), and

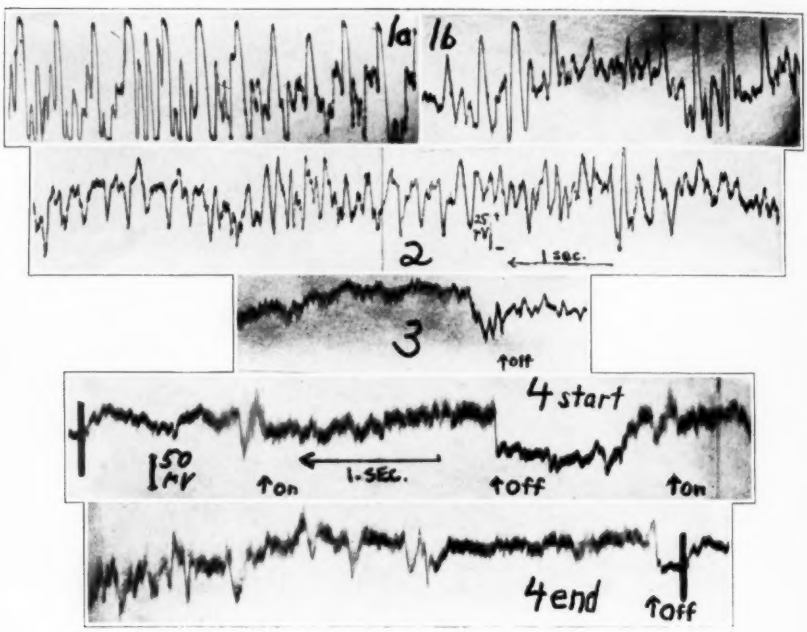

Fig. 5.—Tracing showing optic rhythms. *1* shows slow rhythms in the lateral geniculate body (A8 L8 + 4.5), with the time and voltage similar to those for responses shown in *2*, (*a*) during polarization with a constant current (amplifier overloaded) and (*b*) after polarization, showing beats; *2*, redevelopment of a slow rhythm in the lateral geniculate body (A8 L8 + 4.5) following stimulation with light; *3*, an off response of the lateral geniculate body (A8 L8 + 4) (after intracarotid injection of potassium chloride), followed by return of rapid rhythm, which was inhibited during stimulation with light, the time and voltage being similar to those for responses shown in *2;* and *4*, responses of the optic tract (A9 L8.5 + 2) to two on and off exposures to light. The rapid rhythm is inhibited entirely during illumination, and the rhythm reappears 3.5 seconds after the second off.

from a lead in the radiations a compound wave appeared promptly with light, followed by a similar wave a second later, although the light remained steadily on. The radiations just dorsal to the lateral geniculate body showed, in one instance, three separate bursts following illumination of the crossed eye and three bursts both on illuminating and on darkening the uncrossed eye. From several positions on the lateral and posterior splenial gyri, and especially on the posterior suprasylvian gyrus, such multiple responses were obtained. After on or off stimuli or both, from two to four clearly separate bursts occurred, each burst itself showing considerable complexity of form. In general, the responses from terminal portions of the optic system are more complex than those from intermediate parts, and the responses from primary paths less so.

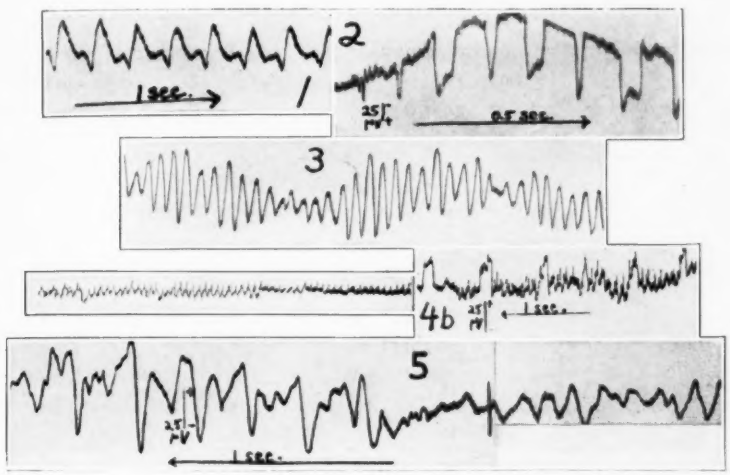

Fig. 6.—Tracing showing spontaneous activity. *1* indicates rhythm obtained from below the nucleus of the inferior colliculus (PO R3 — 1); *2*, rhythm from the basal cerebellar nuclei (P8 L5 + 3); *3*, rhythm from the posterior portion of the vermis (P17 L1 — 5), with the time similar to that for the responses shown in *1*; *4*, (*a*) double rhythm from the optic radiations (A7.5 L7 +6.5) and (*b*) triple rhythm from the lateral geniculate body (A8 L7.5 + 5); and *5*, rhythm waning and waxing in the cortex (A8 L7 + 14).

Optic Rhythms.—The general spontaneous or background activity of various regions of the brain will be considered in the next section, but those which appeared in optic paths, as indicated by activity in response to light, are best considered at this point. Of greatest interest are the many rhythms observed and the influence of optic stimulation on them, but the intensity and frequency of more irregular waves, often characteristically altered on shifting the position of the needle, are also significant. The most striking spontaneous activity of the brain

(except for that of the cerebellum) is a regular rhythm of from 2 to 4 a second found throughout the optic structures.

Especially intense activity in the dark was observed regularly in the cornu, and at least on one occasion each in the hypothalamic commissure, the hypothalamus below the cerebral peduncle and the occipital radiations above the base of the rhinal fissure. Background potentials but a little less intense were obtained from practically the entire optic system, and these were often regular or semiregular rhythms. The latter varied in frequency from 1 in two seconds to 75 a second, but the frequency of the great majority fell between 2 and 4 a second. Often two rhythmic wave trains were present simultaneously at one lead, and then, although not limited to these instances, the potential train waxed

TABLE 1.—*Rhythms at Various Loci*

Structure	Beats per Second
Posterior splenial gyrus	2; 3
Lateral gyrus	1.3; 2.7; 3; 5
Posterior lateral gyrus	2.4 (heart beat 2.7)
Pyriform lobe	2; 3 (sharp)
Posterior suprasylvian gyrus	1.5 (very regular); 1.7; 5
Posterior ectosylvian gyrus (central and deep layers)	4
Suprasylvian sulcus	4
Suprasplenial gyrus and sulcus	1; 3; 3
Radiations	2.1; 2.2; 3; 4
Radiations to lateral gyrus	3.3; 4
Occipital radiations	3
Radiations above geniculate body	1
Tail of caudate nucleus	3
Cornu ammonis	4
Below cornu ammonis	3
Medial geniculate body	4
Lateral geniculate body	0.5; 1; 2; 3.6; 3.8; 4; 6
Reticular substance above optic tract	10
Fornix	2.2 (very regular); 3.2; 3.7
Optic tract	2; 2.2; 2.4; 2.6; 2.7; 3; 3.7; 4

and waned, as in beats between two sounds, for periods of from three to thirty seconds. Such double rhythms were noted in the optic tract, the hypothalamus below the cerebral peduncle, the lateral geniculate body, the tail of the caudate nucleus, the optic radiations, the posterior suprasylvian gyrus and the middle and posterior portions of the lateral gyrus. In this last region were observed in one instance a steady rhythm at a rate of 2.7 a second and a separate volley of regular discharges at a rate of 5 a second, which appeared and disappeared rhythmically. Waxing and waning of regular waves were seen in the posterior suprasylvian and suprasylvian gyri and radiations. One rhythm in the cornu ammonis appeared for three of every ten seconds, and in the lateral geniculate body a regular volley of from 10 to 20 discharges appeared every four seconds. The rates of rhythms observed in various optically active regions are shown in table 1.

The influence of light on this rhythmic activity was predominantly disruptive. Sometimes the background was quieted; more often the

regularity was disturbed, so that asynchronous discharges continued. But in several instances rhythms were intensified or accelerated during, and in many others after, illumination. Especially interesting was a differential effect from the two eyes, in which one stopped and the other enhanced a given rhythm. One point in the posterior splenial gyrus showed a rhythm of 3 per second only in the light and another only in the dark, and a third was practically inactive preceding or during illumination but afterward gave a series of rhythmic volleys, which gradually faded out. At various points in the lateral gyrus rhythms were stopped by light in both eyes or changed in rate or stopped by light in the crossed eye, while increased by light in the uncrossed eye. A point in the gray matter of the suprasylvian sulcus responded to illumination of the eyes with a volley of discharges that became rhythmic and to darkening of the eyes with a new volley, which faded out. Other cortical rhythms were stopped during light. It is probable that these rhythms in the occipital cortex, usually limited in any one cat to an area of only a few square millimeters, are the counterpart of the "Berger" rhythm in man, shown by Adrian and Yamagiwa [19] to originate from a larger circumscribed area.

The radiations above the geniculate body showed a rhythm only when the eyes were dark adapted, those over the rhinal fissure a rhythm intensified by light and those to the lateral gyrus a rhythm unaffected by light in the ipsilateral eye but stopped by stimulation of the contralateral eye, although the optic responses were equally intense from the two eyes. In another case a rhythm of 3.3 per second in the last-mentioned radiations was made irregular by light in the crossed eye but was stopped briefly and then accelerated to 4 per second while the uncrossed eye was illuminated. Other radiations exhibited rhythms stopped by light in either eye, stopped by light in the uncrossed and increased by light in the crossed eye, or stopped during light to return in the dark gradually in from one to five seconds or with a prompt rebound to increased amplitude, rate and sharpness. A similar rebound was seen in the lateral geniculate body. A point in the cornu showed no rhythm in room light, but one appeared three seconds after darkening one eye and seven seconds after darkening both eyes, following a strong off discharge during the intervening time. A regular rhythm of 2.2 a second in the descending portion of the fornix was unaffected by light, although a strong optic response was present.

Especially interesting observations were made on rhythms at various positions in the optic tracts. A clear regular rhythm at 2 a second was stopped by illumination of the contralateral eye and was unaffected by that of the ipsilateral eye. Another double rhythm at 2.2

19. Adrian, E. D., and Yamagiwa, K.: Brain **58**:323, 1935.

a second gradually increased to 2.6 a second and was stopped for only five seconds during continued illumination. Still later the rate fell to 2 a second but rose to 2.3 after illumination. A rhythm at 3 a second was stopped for twelve seconds by light in the crossed eye and then returned at 2.6 a second. Illumination of the uncrossed eye was ineffective at this position, but pushing the electrode a fraction of a millimeter deeper made both eyes act. Another double rhythm at 3.7 a second, showing beats every three to four seconds, was increased during dark adaptation, stopped by light in the crossed eye and increased by light in the uncrossed eye. After light adaptation (atropinized pupil) the rhythm fell to 3.2 a second, and the ipsilateral effect disappeared. A final rhythm at 2 a second appeared for twenty seconds every few minutes with the eyes open to ordinary room light. Flashing light in the contralateral eye rendered this rhythm asynchronous, while in the ipsilateral eye it decreased intensity but left a clear rhythm at 2.4 a second, which rose further to 2.9 a second just after the light was removed. If, instead of an increase in illumination, the eyes were covered, the original rate of 2 a second increased to 2.6 a second for the crossed eye, 2.4 a second for the uncrossed eye and 2.7 a second for both eyes. Later, with light-adapted eyes, the rhythm was 3.5 a second, became asynchronous with light and increased to 4 a second after illumination.

It is difficult to interpret these various effects because of the unknown structural details at the electrode point. Because a rhythm and an optic response are recorded at the same setting is no guarantee that they are present in the same elements, for the electrode must pick up potentials over its entire exposed and relatively enormous surface. This may account for rhythms unaffected by activity of one or both eyes, despite the presence of a good optic response, and for some double rhythms. On the other hand, the observations show, overwhelmingly, interrelations between background and sensory activity and between double background rhythms, so that common neural elements must be involved. It is clear that interaction is present between paths from the two eyes in modulating the spontaneous activity of regions on which they debouch.[20] Possibly the best evidence of this is the change to different rates when the illumination of either one or both eyes is altered, and an opposed action of the two eyes points in the same

20. Gerard and Serota (*Am. J. Physiol.* **116**:59, 1936) showed localized vasomotor changes in optic paths associated with activity evoked by illumination of the eyes. Conceivably, the rhythmic potentials picked up by the needle tip, if near a good-sized blood vessel, could be affected by mechanical factors. Since the separate effects of the two eyes are often unique, the rate of rhythm is altered, light commonly abolishes rather than augments the rhythm and the rhythm is not synchronous with the heart beat, this possibility can be dismissed.

direction. Although the various phenomena can be accounted for in detail by current concepts of convergence and summation, inhibition and the like, it is preferable to note merely that extensive functional interaction must occur between impulses of separate peripheral origin through much of their course in central systems.

Spontaneous Activity.—Without specific stimulation extensive brain regions show continued electrical disturbances, so that a "quiet background" is rather rare. The various afferent (and efferent) systems show, on the whole, great activity, which is but modified by appropriate stimuli. Gray masses often are restless, and qualitatively different activities are readily recognized in different regions. They are described best, perhaps, in terms of what is heard from the loud-speaker, which indicates the degree of rhythm, the volleys and, roughly, the frequency, and characteristic nuances and modulations are readily identified by the ear but are often impossible of verbal description.

The central gray matter below the fourth ventricle gives a "huge" (of maximal intensity) medium-pitched background, sometimes with a semirhythm at 10 a second or with alternate periods of noise and quiet and, in one instance, with a marked rhythm synchronous with the heart beat. The reticular formation of the brain stem is also active, but with less of the slower rhythm and with a more high-pitched background, characterized as "howling." In some cases this drops to a lower-pitched roar or a musical tone; in others it rises to a very high, regular siren note, which may continue steady for some time or fluctuate in pitch or intensity. These discharges of high frequency are especially likely to occur on placing the needle, with the attendant stimulation and injury, but they also appear after such effects are well over. They are most commonly met in the ventral portions of the brain stem.

The tegmentum of the midbrain shows moderate activity, rather greater in the nucleus of the inferior colliculus. In the more superficial part of the colliculus a howling or, more often, a deeply pitched roaring background is present, and in the commissure of the inferior colliculi a clear rhythm of from 15 to 20 a second is observed. The substantia nigra and the nucleus ruber show rather similar intense roaring backgrounds, with a rhythm of a frequency of 100 a second sometimes standing out in the latter region. These structures seem to be especially sensitive to stimulation by the electrode and discharge at a high, siren-like frequency for several minutes after it is placed. In one instance a clear rhythm at 0.8 a second was led from this region of the midbrain. The pons generates a medium or howling background and the brachium pontis a rather rhythmic one, tending to wax and wane. Howls are obtained from the brachium conjunctivum. The cerebellum itself exhibits continued intense activity, often in striking rhythms.

The exploration of this structure, as well as the subjacent more posterior portion of the brain stem, will be reported elsewhere (Gerard and Magoun [21]).

The hypothalamus also exhibits marked activity, varying in different regions. Often a huge roar appears suddenly when the needle reaches this level, continuing in varying quality through its depth. In the region of Forel's decussation the background waxes and wanes, and that about Vicq d'Azyr's bundle is especially active. The supra-optic portion emits rather regular musical howls, often stopped by light. Lateral to the taenia thalami a burst of activity appeared three seconds before a generalized struggle. From the infundibular region sharp diphasic spikes (possibly transmitted muscle potentials) appeared in regular bursts of from 10 to 100 a second. The stimulating effect on placing the needle is documented, in the hypothalamic region, by various autonomic discharges—sudden unilateral or bilateral pupillary changes, either dilatation or constriction, lacrimation and salivation, erection of hair, etc., as well as signs of rage, such as elevation of the nostrils and whiskers, movements of the jaw and tongue (licking) and the like. (A detailed exploration of the exposed median surface of the thalamus and hypothalamus will be reported by Ectors and Brookens.[22]) In an experiment on a monkey a strong rhythm of 5 a second was obtained, probably from the hypothalamus.

The large conducting bundles, especially the medial lemniscus and the cerebral peduncle, show characteristic bursts of activity, which sound as crashes and appear as irregular spikes of high frequency, similar to the reflex discharge in a peripheral nerve. These are added to a background occasionally quiet but often exhibiting regular volleys, howls or even siren tones. The responses of the peduncle, for example, in various experiments were: quiet except for from five to eight volleys at 3.3 per second every one-fourth minute, interrupted at intervals by howls or whistles; almost steady with a siren note, except for occasional crashes, and rhythmical emission of hoarse blasts, sounding like a standing locomotive. Crashes in the motor paths were often associated with spontaneous movements of the body and in a few instances regularly preceded visible movement by a distinct interval, up to a second or two. In the middle portion of the internal capsule in a cat bursts every ten seconds were associated with swallowing movements. The anterior limb discharged from 7 to 10 distinct bursts at accelerating frequency every few seconds. Similar effects appeared in the general radiations, which had a strong, continued, irregular activity, on which were superposed various volley patterns, especially rhythms

21. Gerard, R. W., and Magoun, H. W., to be published.
22. Ectors, L., and Brookens, N.: Am. J. Physiol. **116**:42, 1936.

(mainly in known optic or proprioceptive paths), and bursts, with a gradual start and sudden end, repeated over and over again and sounding as if one train after another were approaching the observer from a distance around a bend. Howls and volleys were also observed in the acoustic radiations. The predominating rhythmic activity in the optic paths has been described, but sharp clicks or volleys or bursts, usually regular (e. g., at 10 a second), also appeared in the chiasm or optic tracts. The corpus callosum was only moderately active, giving a rather low-pitched, hollow, rumbling background.

Strong activity in the thalamus is associated with the various afferent systems but is also obtained at needle positions not showing a response to specific stimuli. The nucleus of the lateral geniculate body is intensely active, with a semirhythm, and the medial geniculate body less so, and the near-by ventrolateral nucleus gives a loud rumble, appearing suddenly as the needle enters it from above. A similar, less intense background appears on entering the dorsal thalamic nucleus. The lateral and the anterior ventrolateral thalamic nuclei are very active, with frequent rhythms and volleys, and the medial nucleus is less so. Ventrolaterally, rhythmic volleys appeared for four seconds every half minute independent of cutaneous stimulation, or they were initiated by this stimulation, or, in the ventral medullary layer, they were stopped by pinching the hindleg. The more dorsal part of the lateral nucleus gives a roar, sometimes low pitched and semirhythmic, which ends sharply as the needle penetrates farther. The more ventral part characteristically shows regular rhythms and volleys. The following were observed in different cats: a sharp rhythm at 10 a second, appearing for from one to two seconds every ten to twenty seconds; a continued rhythm at 8 a second; a rhythm at 3 a second, lasting twenty seconds; strong volleys at 10 a second, and volleys at 3 a second, superposed on a double rhythm showing beats. A rhythm at 85 a second was obtained from the lateral portion of the thalamus in one instance and at 70 a second in another.

The caudate nucleus also tends to discharge volleys on a background of continuous activity. These may be irregular or may appear every five to ten seconds, and there may be a regular rhythm at 20 a second, or one at 60, which waxes and wanes over a period of from two to three seconds. Volleys, associated with tactile tracts, appear in the putamen. Activity in the cornu ammonis is closely related to light; no rhythms uninfluenced by illumination were noted. In one instance a strong rhythm like that of a standing locomotive was present, which became intermittent while the light was on.

Activity in cortical regions has often been described. Our observations, made with concentric electrodes, were of highly localized potential differences well within particular cyto-architectural areas rather

than of the potential swings of whole masses. Many observations were made with surface contact only, others on penetration. The posterior olfactory lobe and rhinal cortex gave a low-pitched howl, with a rhythm of 10 a second or volleys, in one case from 7 to 10 discharges at increasing frequency repeated every seven seconds. The splenial sulcus gave a loud, deep-pitched background, with an added rhythm of 50 a second, and a rhythm (optic) waxed and waned in the posterior splenial gyrus. A loud, rumbling, semirhythmic background appeared suddenly on entering the fornicate gyrus from above. The posterior lateral, ectosylvian and sylvian gyri showed moderate activity with volleys (not sensory) and occasional crashes, the active portions often ending with a sharp boundary, especially at the gray-white junction. The surface of the suprasylvian gyrus gave an irregular rhythm plus volleys every five seconds, and extra bursts preceded body movements. Deeper were obtained a musical howl, irregular volleys and a background which waxed and waned in groups at four second periods. The posterior suprasylvian gyrus gave a regular rhythm close to that of, but definitely out of phase with, the heart beat, and from the white matter below regular volleys at 10 a second were obtained.

The monkey cortex was also active. In one instance a sudden burst in the striate cortex preceded a general struggle. Continued activity of the background was present in the optic and, particularly, in the auditory and somesthetic projection areas. It was less intense in the motor region, and association areas were, in general, still less active. Large waves in the cerebellum were observed in this animal as well as in the cat.

Other Observations.—Scattered observations on spontaneous or evoked potentials are briefly noted here. In one monkey and one cat (no others were tried) traction on the liver led to marked activity in the hypothalamus, as well as to motor signs of sympathetic discharge (dilatation of the pupil, erection of hair, etc.). In the monkey regular potentials at 65 a second were evoked; in the cat strong initial bursts at each traction settled into a rhythm of 3 a second which lasted from five to thirty seconds.

In a few trials olfactory stimuli (asafetida, alcohol and ammonia) evoked large, slow waves lasting from one-tenth to two-tenths second, in the habenular nucleus.

Rhythms synchronous with that of the heart beat or the respiration were commonly encountered and in most cases were discarded as artefacts, owing to the regular movement of tissue (brain in mass or local arterial pulsing) against the electrode tip. In a few cases these rhythms were strong and sharply localized, and the potential changes were not the slow, regular ones characteristic of continued movement but volleys;

so they represent discharging centers or tracts controlling these functions. Such pulse rhythms were encountered in the gray floor of the fourth ventricle, once in the reticular formation and once in the thalamus, when a sharply localized rhythm which waxed and waned over one-half to one minute intervals was synchronous with the heart beat. Respiratory rhythms were encountered in the medulla; in a monkey sharp, diphasic spikes (over 70 microvolts) at from 30 to 80 a second occurred with each respiration and increased during asphyxia, and similar spike discharges preceding each inspiration were seen in the cat. Less sharp respiratory discharges were also encountered in the cerebral peduncle and near the lateral lemniscus in the midbrain.

Action of Anesthetics and Other Agents.—Three anesthetics were used in these experiments: tribromethanol in amylene hydrate, pentobarbital sodium and ether. We did not note any consistent differences in the electrical activity of the nervous system under the influence of one drug or another. In all cases light doses had little observable effect (although an initial augmentation of background often appeared); moderate doses somewhat depressed the spontaneous rhythmic activity, and only very deep anesthesia abolished the potentials evoked by sensory stimulation, as well as the spontaneous potentials. Ether was mostly superimposed on one of the other drugs in these observations on the effect of the depth of anesthesia.

A strong rhythm in the optic chiasm of from 10 to 15 a second was abolished in four minutes with full ether anesthesia (tracheal cannula) and returned in half a minute after the administration of ether was stopped. In another cat a semirhythmic background in the chiasm was first increased and then lessened, with the rhythm left more pronounced, by progressively increased doses of ether. After return to the initial conditions an additional injection of pentobarbital sodium abolished the rhythm. Responses to light were unaffected throughout.

Background activity and volleys in the lateral geniculate body were increased by light ether anesthesia and were unaffected by pentobarbital sodium. Rather irregular volleys in the radiation to the posterior suprasylvian gyrus appeared every ten seconds without ether. With the animal under moderate ether anesthesia these became sharper and more regular and with a beat every five seconds. In the acoustic radiations, likewise, spontaneous volleys and auditory potentials were not abolished by moderate ether anesthesia. An irregular rhythm with volleys every five seconds, obtained from the cortical surface of the suprasylvian gyrus, was progressively decreased with increased administration of ether. The response to light, however, was rather suddenly abolished after four minutes of full ether anesthesia and returned in thirty seconds with no ether, as in the case of the chiasm. Auditory responses from the thalamus were lost and returned similarly. In the monkey a rhythm of 5

a second in the lower portion of the thalamus was cut to 20 per cent of its initial intensity by full ether anesthesia in two minutes. A more complete protocol for the basal gray matter of the cat (table 2) shows clearly an early stimulating and a later depressing action of ether on a spontaneous rhythm. The whole sequence was repeated twice more on this cat, with similar results; so there is full reversibility.

Alcohol (1.5 cc. of 40 per cent) depressed optic (and auditory) responses from the radiations to 80 per cent twenty seconds after intravenous injection. Seven minutes later a further injection of 2 cc. practically abolished the responses in thirty seconds and depressed respiration. After three minutes definite recovery occurred, and after seven minutes the responses were back to half their original intensity.

Carbon dioxide blown against the optic cortex gave a definite increase in the cortical response to illumination of the eyes. Stronger concentration of carbon dioxide on inhalation decreased or abolished optic responses in the radiations and colliculus, which fully returned after its removal. Since these responses were absent at a time when

TABLE 2.—*Effect of Ether on Rhythm in the Basal Gray Matter* *

Anesthesia	Rhythm	
	Rate per Second	Amplitude, Mm.
Light	60	15
Full, 5 min.	40	8
None, 2 min.	50	24
None, 5 min.	55	15
Full, 4 min.	54	20
Full, 7 min.	Irregular and feeble	
Full, 9 min.	None	None

* It was possible to reverse this whole sequence twice.

marked hyperpnea was present, it seems that various neural regions are at least quantitatively different in their sensitivity to carbonic acid. Auditory responses to the watch tick and metronome beat were transiently increased and then markedly depressed by carbon dioxide, and the form of the wave was modified. The peak response, 25 mm., to a metronome beat was cut by a moderate concentration of carbon dioxide to 15 mm., and many beats were almost or entirely missing on the tube face. The changed response to a watch tick is indicated in the rough tracings shown in figure 1.

Marked changes in background and evoked potentials can also be induced by local or intravenous administration of potassium, calcium or citrate ions, by increase or decrease in the blood sugar content, by changes in temperature and by polarization of the brain with direct currents, but these will be reported more fully elsewhere (Gerard [23] in collaboration with Dubner).

23. Gerard, R. W.: Tr. Am. Neurol. A., to be published; Cold Spring Harbor Symp., Quant. Biol., to be published.

Responses to light and sound were obtained by means of concentric electrodes from human brains exposed for operation, with the patients under local anesthesia (with the cooperation of Dr. Bailey and Dr. Case), but electrical disturbances in the operating room excluded adequate study at that time. Further experiments on the influence of polarization, carbon dioxide, hormones and hypnotic suggestion on brain potentials in the human subject, likewise directed toward the analysis of factors determining the automatic activity of nerve cells, are also in progress (Gerard [23] in collaboration with Blake).

COMMENT

The data presented, aside from their usefulness in mapping conducting and rhythmically active brain systems by the potential method and so affording a more exact anatomic basis for further investigations, touch on a number of important questions. It is worth emphasizing, first, that high degrees of localization are possible, certainly, within the conducting systems and, to a less extent, in the cortex itself. In the quadrigeminal region and in the lateral portion of the thalamus it has been possible for concentric electrodes to pick up visual and auditory potentials sharply separated within 1 mm., and equivalent sharpness is obtainable through most of the thalamic and projection systems. In the cerebral cortex it has been shown by Kornmüller and Tönnies (Kornmüller [24]) that the separate architectonic regions have their characteristic potential patterns, with sharp delimitation of the boundaries. Each region does not, however, act in accurate unitary fashion, for if it did we should have been unable to record any changes in potential with the concentric needle. Since this is possible for both spontaneous and evoked potentials, differences must be set up over a distance of a fraction of 1 mm., even within a single area.

It does not necessarily follow that central neural function is primarily a mosaic built of the activity of separate small units. In fact, not only the earlier experiments of Lashley,[25] indicating a mass function, and the phenomena emphasized by the *Gestalt* school, which point in the same direction, but direct observations of massive electrical changes, such as those by Berger [26] and Adrian,[19] afford ample evidence that this is not the case. The more massive activity will be discussed further, but it is worth emphasizing that even if specific responses depend on nonlocalized but characteristic activity patterns it would still be necessary that incoming impulses be accurately localized and definitive up to

24. Kornmüller, A. E.: (*a*) Biol. Rev. **10**:383, 1935; (*b*) Fortschr. d. Neurol., Psychiat. **7**:391 (Sept.); 414 (Oct.) 1935.

25. Lashley, K.: Brain Mechanisms and Intelligence, Chicago, University of Chicago Press, 1929.

26. Berger, H.: Naturwissenschaften **23**:122, 1935.

the point where they debouch into the general pool. Such localization would surely be present largely in the afferent and efferent conducting systems and could extend in detail to the well known primary projection areas, or even farther. This would not lessen the possible importance of later mass responses, no longer localized as to the specific neural elements involved, although still possessing definitive patterns.

The strikingly low threshold for afferent impulses is further evidence of localized pathways. There seems to be little doubt that the threshold for a conscious awareness of sensation is at least not lower than that for eliciting electrical responses in or close to the cortex (section on anesthesia in this paper and Dubner, Gerard and Kobrak [27]). The paths from end-organ to sensorium are consequently open and show little evidence of successive levels of synaptic resistance at which impulses must progressively summate to get through. Reference has already been made to clearcut responses in the thalamus from light touch of a single hair on the leg. Here, surely, one or very few receptors discharge at relatively low frequencies; yet the impulses ascend the whole neuraxis with no difficulty and even engage many parallel neurons. Again, it appears that precise through-paths to the cortex are available to incoming stimuli, whatever their fate after arrival.

In partial contrast to the quantitative ease with which impulses reach the hemispheres is the relatively long latent period often observed. Delays of five hundredths of a second between the stimulus and the central electrical response are not uncommon, although hardly one fifth of this time could be accounted for by conduction in fibers, even at velocities of 30 meters a second. Whether the delays occur at cells or at synapses, whether they may be accounted for by still slower conduction rates or whether much of the time elapses in the receptors themselves cannot be answered from our data.

Berger,[28] especially, emphasized the bearing of studies of brain potentials on the question of anesthesia and reviewed the evidence for the existence of two distinct types. Drugs of the barbiturate series, on the one hand, are supposed to block incoming impulses, presumably at the thalamic level, while ether and other nonbarbiturates are effective by directly depressing cortical activity. In the former instance cortical potentials become larger and more regular and are no longer modified by afferent stimulation; in the latter the normal potentials are progressively decreased as response to stimulation is also lost. Our own findings are not fully in accord with this view. Tribromethanol, ether and the barbiturate pentobarbital sodium, alone or in combination, appear to

27. Dubner, H.; Gerard, R. W., and Kobrak, H.: Am. J. Physiol. **116**:38, 1936.

28. Berger, H.: Arch. f. Psychiat. **101**:452, 1933.

have little or no influence on the ability of incoming impulses to reach the corona radiata or the cortical surface until their administration is pushed far beyond that necessary for ordinary surgical anesthesia, to a point at which the spinal and corneal reflexes are lost and respiration is about to fail (compare these results with those of Forbes and his co-workers [29]). At this point conducted potentials are suddenly lost, and the whole picture is strikingly like that of a peripheral nerve in obeying the all-or-nothing law. The spontaneous potentials, on the contrary, are progressively affected by increasing anesthetic doses and become feebler and slower, after an initial increase, as anesthesia is pressed. If it is assumed that the spontaneous potential rhythms originate in the nerve cells themselves and are not an expression of unrecognized reflex activity, this behavior becomes understandable.

The evoked activities continue as long as conduction in fibers and across synapses is possible and, if picked up from conducting fibers, are as intense as the physiologic state of these fibers permits. Since anesthetic doses of these drugs are far below the amounts required to depress nerve fibers seriously, the impulses measured will remain practically maximal until block occurs somewhere along the way, possibly at synaptic junctions or in cell bodies. The cell potentials, on the contrary, should show progressive depression, since nerve cells apparently do not obey the all or nothing law and since anesthetics in the concentrations used affect them. As conducted impulses appear to pass through the whole afferent system with little need of summation, they should come through depressed cells or synapses as through a depressed stretch of nerve and, until block occurs, should still be maximal in the fiber tracts from which they are recorded.

There remains the intriguing question of how the anesthetic state arises—of where or how the block occurs between impulses in the cortical projection areas and a conscious awareness of sensation. It may be assumed that a subsequent stage is interfered with, one possibly associated with nonlocalized activity patterns.

Interaction between separate evoked potentials is of interest. In favorable locations, such as regions between the two colliculi or the two geniculate bodies, excitation of one sensory system increases the responses to the constant stimulation of a second. Thus, regular watch ticks evoke larger, but otherwise unmodified, potential changes in the brain stem when the eyes are simultaneously exposed to light than when the subject is in the dark. Since the potential picture evoked in optic paths by light is distinct from that in the auditory paths, the explanation is clearly not a simple addition of active optic to active auditory struc-

29. Forbes, A.; Derbyshire, A. J.; Remple, B., and Lambert, E.: Am. J. Physiol. **113**:43, 1935.

tures. Rather, secondary auditory paths have somehow been facilitated, so that more fibers are activated by a given discharge in the primary paths. It would be fruitless at present to speculate on the mechanism of this interaction, except to note that it occurs where optic and auditory systems are in close anatomic relation, although presumably it does not involve the cross-passage of nerve impulses over synapses between them. It affords, perhaps, an additional example of the synchronization of elements, to be discussed later, and it may further give a clue to the mechanism of establishing conditioned reflexes, for the latter clearly depend on the formation of effective connections between two regions of the brain which are repeatedly thrown into simultaneous activity. The simple interactions described are perhaps a prototype of these connections. Interactions within one system, such as a decrease in latency or the specific effects on the optic rhythm when both eyes are illuminated, as compared with the effect of either eye alone, and the engagement of parallel ascending neurons by impulses from a single tactile receptor, have been considered in the text.

We have called spontaneous the more or less regular potential waves observed widely throughout the brain in the absence of deliberate stimulation. This is meant to imply activity which is not evoked by nerve impulses impinging on the active system. Our own experiments do not exclude the presence of reflex activities of many sorts, but it is unlikely that these play a marked rôle in determining the spontaneous potentials observed. The observations of Bremer [30] and of Adrian and Buytendijk [31] on the isolated cerebrum or neuraxis, for example, emphasized the origin of these potentials within the neural mass, and the great bulk of other experimental data indicates that afferent impulses tend to break up rather than to augment these rhythms. Gerard and Young [12] observed strong rhythmic potentials in the isolated frog cerebrum, especially from the olfactory bulb. It is not vital to the present considerations whether the spontaneous potentials are recorded from cell bodies, dendrites or medullated axis-cylinders or whether wave shapes differing from spikes to slow sinusoidal changes are to be correlated with separate types of elements (Adrian and Matthews [32]).

The crucial point is whether or not individual neurons exhibit a spontaneous rhythmic activity, manifested at least electrically. Such activity has long been attributed to the respiratory center in vertebrates and has been shown unequivocally in the insect. Brevée and Dusser de Barenne [33] observed similar rhythmic discharges of anterior horn cells

30. Bremer, F.: Bruxelles-méd. **16**:330 (Dec. 29) 1935.
31. Adrian, E. D., and Buytendijk, F. J. J.: J. Physiol. **71**:121, 1931.
32. Adrian, E. D., and Matthews, B. H. C.: J. Physiol. **81**:440, 1934.
33. Brevée, J. F. G., and Dusser de Barenne, J. G.: J. Physiol. **61**:81, 1926.

after blocking their afferent connections with local anesthetics. Synchronous discharges from the isolated retina of the eel were obtained with steady, uniform illumination by Adrian and Matthews,[34] and Kornmüller [24a] and Tönnies emphasized the characteristic potential patterns appearing in individual cyto-architectural areas of the cortex. Bartley and Bishop [35] observed a rhythm of 5 a second in the optic cortex of the rabbit, and Berger [26] a rhythm of 10 a second in the human being, which Adrian and Yamagiwa [19] also located primarily in the visual cortex. We had similarly observed a rhythm of from 2 to 4 a second in the cat, involving not only the striate cortex but the entire optic system as well. These rhythms in most instances are diminished in amplitude, broken into irregular fragments, with an increased frequency of small waves, or abolished entirely by active stimulation or, in the case of man, by concentrated thinking. (Gerard [23] and Blake, and Loomis and his co-workers [36] found that these effects can be duplicated by suggestion with the subject under hypnosis.) We have observed several cases, however, in which the optic rhythm was increased during illumination, and Loomis, Harvey and Hobart [36] reported that sound stimulation evokes fairly regular potential trains in the electrically quiescent brain of a sleeping man. This latter rhythm, although differing in frequency and region of maximal intensity from the normal waking one, may still be due to partial awakening rather than to a specific auditory effect. We also observed regular highly localized potential rhythms in the hypothalamus and medulla synchronous with, but not produced by, respiratory movements or heart beats and sudden marked potential discharges related to, but definitely preceding, general struggling movements.

The weight of evidence, therefore, strongly suggests that individual neurons possess the property of rhythmicity and tend to "beat," as does the pacemaker of the heart. The individual cells, moreover, tend to keep in pace with their neighbors, often over long distances, and especially so under the influence of convulsant drugs or other conditions of heightened irritability, such as mass polarization with a constant current (Gerard [23]). Such coordinated discharges often involve the bulk of the cells not only of one center but of the contralateral centers. Discharges over both phrenic nerves, for example, tend to be in duplicate (Gasser and Newcomer [37]), as do reflex vasomotor discharges in the cervical portion of the sympathetic trunk (Bronk [38]). The coordination

34. Adrian, E. D., and Matthews, R.: J. Physiol. **65**:273, 1928.

35. Bartley, S. H., and Bishop, G.: Am. J. Physiol. **103**:159, 1933.

36. Loomis, A. L.; Harvey, E. N., and Hobart, G.: J. Exper. Psychol. **19**: 249, 1936.

37. Gasser, H. S., and Newcomer, H. S.: Am. J. Physiol. **57**:1, 1921.

38. Bronk, D. W.: The Nervous Mechanism of Cardio-Vascular Control, Harvey Lectures, 1933-1934, Baltimore, Williams & Wilkins Company, 1935, p. 245.

of separate neurons beating together can hardly depend primarily on the usual nerve impulses conducted along collateral connections from cell to cell. Although stimulation can increase rhythms, this is probably secondary to a general enhanced excitability, since the effect outlasts and even increases after the stimulus. Similar cerebellar rhythms have appeared after electrical stimulation (Gerard and Magoun [21]), and it seems as though a mild play of afferent impulses facilitates the beat of single cells and a stronger afferent discharge disrupts the synchrony of many cells. Nerve impulses would be, on the one hand, too slow to permit the essential simultaneity of discharge of cell masses and, on the other hand, too fast to account for the slow spread of waves of electrical activity in the "convulsing" cortex. Conduction of nerve impulses would likewise account poorly for the steplike spread of these potentials in sweeping over one cyto-architectural area at a time, as reported by Kornmüller [24b] for the rabbit brain. (Gradual spread, due to facilitation within partly "closed circuits" [Herrick,[39] Kubie,[40] Ranson and Hinsey [41] and Lorente de Nó [42]] might help in this connection.) Most direct evidence comes from the observation of Adrian and Matthews on the retina that the synchronous discharge obtained with even illumination is completely destroyed by the presence of even a small pattern in the visual field. It seems impossible to account for this by the usual theory of particular nerve impulses traveling along particular paths. The work of Weiss,[43] showing that nerves connected with different individual muscles carry impulses only when the nerve to the normally innervated muscle of the same type also carries them, points in the same direction. It suggests that one pattern of activity in the central nervous system engages particular motor neurons, and another pattern, others, irrespective of their particular anatomic position. Lashley's evidence of "mass action" in the cerebrum affords further data that seem to demand a similar type of interpretation.

What the mechanism for this "distance action" is, if conducted nerve impulses are to be excluded, remains to be analyzed. The possibility has often been suggested that the potential changes themselves afford a coordinating mechanism. Lillie's [44] observation on the simultaneous lashing of spermatozoan tails and the simultaneous discharge of individual nerve fibers arising from the cut end of an isolated nerve

39. Herrick, C. J.: Brains of Rats and Men, Chicago, University of Chicago Press, 1926, p. 317.

40. Kubie, L. S.: Brain **53**:166, 1930.

41. Ranson, S. W., and Hinsey, J. C.: Am. J. Physiol. **94**:471, 1930.

42. Lorente de Nó, R.: J. f. Psychol. u. Neurol. **45**:381, 1934.

43. Weiss, P. A.: J. Comp. Neurol. **61**:135, 1935.

44. Lillie, R. S.: Protoplasmic Action and Nervous Action, Chicago, University of Chicago Press, 1932.

(Adrian [45]) perhaps point the way. Especially striking is the finding of Barron and Matthews [46] that impulses in nerve fibers traversing the cord without synapse can be periodically blocked and that depressing the activity of the cord, as by cold, abolishes the blocking rather than the impulses. Here again, the facts suggest much more strongly a mechanism of an electrotonic type than one of impulse interference of the Wedensky type. It has, in fact, proved possible to alter greatly spontaneous rhythms in the cat or human brain by passing through it a polarizing current that had no effect on the evoked potentials (Gerard [23]).

A new picture of neural function is thus beginning to emerge from recent experimentation. In the central nervous system, and particularly in the cortex, patterns of activity, in addition to the locus of activity, seem to be important. The spontaneous beating of individual cells is coordinated, apparently in large part, by unknown mechanisms, so as to produce synchronization of smaller or larger masses. These relatively local rhythms are in turn played on by the activity of other regions, mainly perhaps by means of nerve impulses traveling in well recognized tracts. The activity of "lower" centers is thus ordinarily subordinate to that of "higher" centers, which dominate them. This relation of dominance, clearly stated by Hughlings Jackson, is borne out for the nervous system by a great wealth of clinical and experimental data (for example, spinal and hypothalamic release phenomena), as well as for the whole organism and other organ systems (Child [47]). On the resultant complicated pattern of the "resting" nervous system plays in turn the whole array of incoming impulses, themselves already organized into fairly complex patterns in the afferent systems (Dusser de Barenne [48] and Stopford [49]). The relative equilibrium is displaced in characteristic manner; new constellations of activity appear; coordinated patterns of motor discharge result, and a new state of equilibrium is attained, only to suffer renewed displacement.

On the motor side such a pattern of equilibrium and its change with activity to a new one are well established in relation to postural reflexes and movements. In relation to consciousness, likewise, the modern dynamic picture of psychic processes as in continuous flux, whether "conscious" or "unconscious," is in accord with such a view of neural mechanisms. The beat of single neurons and their integration as small

45. Adrian, E. D.: Proc. Roy. Soc., London, s.B **106**:596, 1930.

46. Barron, D. H., and Matthews, B. H. C.: J. Physiol. **85**:73, 1935.

47. Child, C. M.: The Origin and Development of the Nervous System, Chicago, University of Chicago Press, 1921.

48. Dusser de Barenne, J. G.: Central Levels of Sensory Integration, Arch. Neurol. & Psychiat. **34**:768 (Oct.) 1935.

49. Stopford, J. S. B.: Sensation and the Sensory Pathway, New York, Longmans, Green & Co., 1930.

and large groups into a pattern of activity, perhaps involving the whole brain, give a basis for the unity of normal consciousness and its continued modulation by external stimuli and internal states. Anesthesia, for example, while not blocking afferent impulses, may none the less suspend awareness by lessening cellular activity or disrupting the whole active pattern.

It should perhaps be emphasized that this more fluid picture of central nervous activity, far from being alternate to the long-current ideas of well localized tracts and connections, is predicated on them, for only on the basis of preexistent connections and established activity patterns could reproducible and coordinated activities exist.

In conclusion, it is of interest to consider the source of the rhythmic activity of nerve cells. As Lillie [44] emphasized, rhythmic action must depend on steady underlying conditions. The nerve cell rhythm must somehow be an expression of the steady metabolic activity of the cell. This is temporarily modified by excitation by way of impinging nerve impulses. It would be more continuously dependent on the steady condition of its environment, and so indirectly on the blood stream. Much evidence already exists to show the dependence of particular nerve centers on particular attributes of the blood. One need only recall the action of acid or carbon dioxide on the respiratory and vasoconstrictor centers, of excess of calcium or potassium on the hypothalamic "sleep center," receptors, etc. (Hoagland [50]), of increase or decrease in the temperature of the blood or in the blood sugar content on the activity of the thermoregulatory and glycemic centers and of the general convulsions accompanying a diminished amount of blood calcium, and the like, to be impressed by the intimate control exerted by the environment of the nerve cell on its activity.

It seems probable, indeed, that the "specific" response of different centers to given conditions of the blood is mainly quantitative. The respiratory center, for example, differs from the mass of the nervous system in its sensitivity to carbon dioxide more in degree than in kind. In addition, however, there is a strong suggestion that different nerve cells have qualitatively different metabolisms, so that a given environmental change leads to opposed changes in activity. Thus, the thermogenic center seems to be stimulated by decrease in temperature, in contrast to most of the nervous system, and orthosympathetic and parasympathetic centers give opposite responses to a given shift in the potassium-calcium ratio or in the sugar concentration in the blood.

50. Hoagland, H.: Pacemakers in Relation to Aspects of Behavior, New York, The Macmillan Company, 1935.

TABLE 3.—*Data for Figure 7*

A	L	±	Structures	
15.6	15.0	8.0	Anterior ectosylvian gyrus	
15.6	13.0	1.0	Anterior sylvian gyrus	
15.6	12.0	15.0	Median suprasylvian gyrus	
15.6	12.0	10.0	Suprasylvian sulcus	
15.6	12.0	5.0	Ectosylvian sulcus	
15.6	11.0	—1.0	Rhinal sulcus	
15.6	10.0	2.0	Anterior portion of claustrum	
15.6	10.0	—4.0	Pyriform lobe	
15.6	9.0	3.0	External capsule	
15.6	8.0	2.0	Putamen	
15.6	7.0	15.5	Lateral sulcus	
15.6	7.0	12.0	Corona radiata	
15.6	7.0	—3.0	Amygdala	
15.6	7.0	—6.0	Olfactory radiations	
15.6	6.0	10.0	Subcallosal stratum	
15.6	6.0	3.0	Anterior limb of internal capsule	
15.6	6.0	0.0	Globus pallidus	
15.6	4.0	18.0	Lateral gyrus	
15.6	4.0	16.0	Suprasplenial gyrus	
15.6	4.0	14.5	Splenial sulcus	
15.6	4.0	10.0	Lateral ventricle	
15.6	4.0	6.0	Head of caudate nucleus	
15.6	1.0	15.0	Fornicate gyrus	
15.6	1.0	11.0	Rostral gyrus	
15.6	1.0	8.0	Corpus callosum	
15.6	1.0	4.0	Septum pellucidum	
15.6	1.0	0.0	Anterior commissure	
15.6	1.0	—2.0	Hypothalamus	
15.6	1.0	—5.0	Optic decussation	
15.6	0.5	2.0	Descending column of fornix	
			Auditory Responses	
16.0	12.0	S	Response	
			Somesthetic Responses	
15.5	14.0	10 to 8	Crossed forepaw response	
15.5	12.0	14 to 6	Crossed forepaw response	
15.5	10.0	17 to 3 7 M	Volleys and response from forelegs	
15.5	10.0	13 to 4	Crossed forepaw strongest, others present; volleys on touch	
17.0	8.5	11 to 3	Response from bending legs; volleys	
15.5	8.0	14 to 5 8 M	Crossed forepaw strongest, others present; volleys on touch and sustained discharges on holding jaw open	
15.5	8.0	4 to 2	Touch from crossed forepaw, less from uncrossed; strong volleys	
15.5	6.0	13 to 11	Crossed forepaw response; volleys	
15.5	4.0	8 to 8	Response from legs	
			Optic Responses and Rhythms	
16.0	6.0	—5.0	Response	
16.0	4.0	—5.0 to —6.5 M	Very strong on and off responses and after discharge	Rhythm
16.0	2.0	—5.0	High-pitched response and long after-discharge	Rhythm
15.5	2.0	—7.5	On and off responses	Background increased by more ether and decortication, leaving rhythm and response unchanged; further administration of ether decreased background, bringing out rhythm; pentobarbital sodium finally stopped rhythm
			Spontaneous Activity	
15.5	12.0	6.0 to 5	Volleys	
17.0	8.5	11.0 to 3	Rhythm (in proprioceptive paths)	
15.5	8.0	15 0	Irregular volleys	
15.5	8.0	3.0	Loud volleys (partly tactile)	
15.5	6.0	4.0 to 3	7 to 10 accelerating volleys every few seconds	
15.5	4.0	11.0	Sharp change in background	
15.5	4.0	10 0 to 8	Volleys	
15.5	4.0	10.0 to 8	Howl	
15.0	4.0	9.0	Sudden decrease in background	
15.0	4.0	7.0	Volleys every 5 to 10 seconds	
15.0	4.0	4.0 to 3	Localized increase in volleys and background	
15.5	4.0	0.0	Roar every 10 seconds and accompanying swallowing movements	
15.0	3.0	—2.5	Musical note and howl	
15.0	2.0	—7.5	Background	

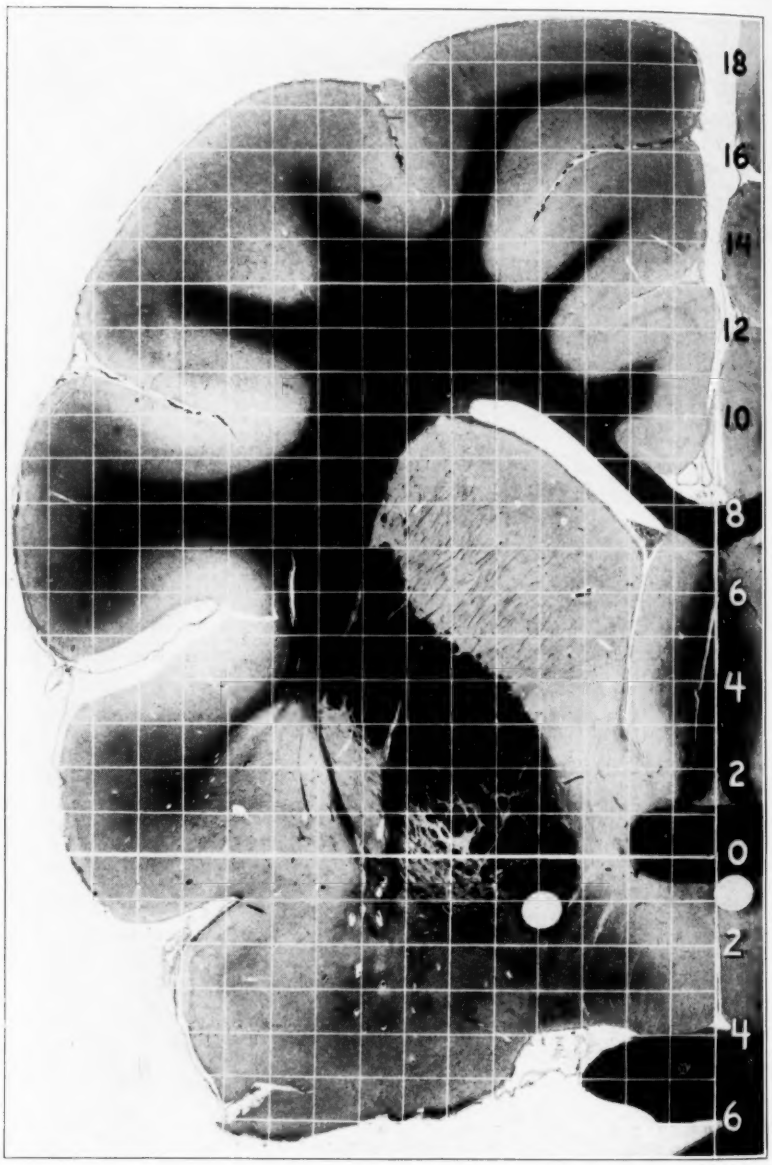

Fig. 7.—Photomicrograph of a section of the cat's brain in the frontal plane of the Horsley-Clarke instrument, 15.6 mm. in front of the interaural line.

TABLE 4.—*Data on Figure 8*

A	L	±	Structures	A	L	±	Structures
13.6	12.0	1.0	Extreme capsule	13.6	5.0	—3.0	Optic tract
13.6	12.0	—3.0	Rhinal sulcus	13.6	5.0	—6.0	Posterior olfactory lobe
13.6	11.0	2.0	Claustrum	13.6	3.0	1.0	Ventral portion of lateral nucleus of thalamus
13.6	11.0	—6.0	Pyriform lobe				
13.6	10.0	—4.0	Anterior commissure	13.6	2.0	5.5	Head of anterior nucleus of thalamus
13.6	9.5	0.0	External capsule				
13.6	9.0	2.0	Putamen	13.6	2.0	—2.0	Hypothalamus
13.6	9.0	—5.0	Amygdala	13.6	1.5	6.5	Fornix
13.6	8.0	1.0	Globus pallidus	13.6	1.5	—2.0	Descending limb of fornix
13.6	6.0	—1.0	Globus pallidus	13.6	1.0	4.0	Taenia thalami
13.6	5.5	10.5	Subcallosal stratum	13.6	1.0	1.0	Vicq d'Azyr's bundle
13.6	5.0	8.0	Body of caudate nucleus	13.6	1.0	—4.0	Medial infund.bular nucleus
13.6	5.0	5.0	Thalamocortical radiations	13.6	0.0	—4.0	Anterior portion of infundibulum
13.6	5.0	4.0	Anterior portion of lateral nucleus of thalamus	13.6	0.0	—6.0	Hypothalamic commissure and decussation (Meynert)
13.6	5.0	0.0	Internal capsule				

			Auditory Responses		
12	12.0	15 to 7	9 M	Very sharp response	
			Somesthetic Responses		
13.5	14.0	9 S to 6		Forepaw, faint response	
13.5	12.0	S to 11		Crossed shoulder; none from paw; volleys	
13.5	12.0	8 to 6		Crossed forepaw	
13.5	10.0	S to 5		Crossed forepaw; touch response and volleys	
13.5	8.0	12 S to 2	5 M	Crossed forepaw; touch and volleys very strong; disappeared sharply at 2	
13.5	6.0	8		Both forepaws and crossed hindpaw; touch	
12.0	5.0	2 to 0		Crossed foreleg and some from uncrossed foreleg; toes squeezed or stretched	
13.5	4.0	—1		Jaw; discharges when held open	
			Optic Responses and Rhythms		
12.0	8.0	5.0		Fair response, multiple volleys; a second response 1 sec. later	Rhythm 2.2 a sec.
12.0	5.0	6.0 to 4.0		—	Rhythm every 10 sec.
14.0	5.0	0.0		Response	Rhythm of 10 a sec., waxing and waning every 30 sec.
12.0	5.0	—4.0		Crossed response greater than uncrossed	Very regular rhythm of 2 a sec., stopped by light in crossed eye
12.0	5.0	—5.0		Crossed response only	Very regular rhythm of 2 a sec., stopped by light in crossed eye
12.0	5.0	—7.0		Strong response	—
12.0	4.0	S to 9.0		Response	—
12.6	3.0	—5.0 to —7.0		Response	—
12.0	2.0	—6.0		Response	Rhythm not stopped by light
14.0	1.5	—3.0 to —5.0	M	Response abruptly out at —5, base at —7	—
13.5	1.5	—4.0 to —5.0		Good bilateral response	—
13.5	1.5	—5.0		Good bilateral response	Sharp clicking rhythm, 2-3 a sec. at —5
14.0	1.0	—1.0 to —6.0	—5.5 M	Strong response and after-discharge for 2 min.	—
12.0	1.0	—4.0		Very slight response	—
12.0	1.0	—6.5		Response	Rhythm
13 0	0.5	—6.0		Response	Rhythm
14.0	0.0	—5.0 to —6.5		Moderate response	—
14.0	0.0	—5.0		Strong response	Strong rhythm stopped by light in crossed and uncrossed eyes
			Spontaneous Activity		
13.5	6.0	4.0 to 2.5		Very strong volleys	
12.5	5.0	9.0		Rhythm 20 a sec.	
12.5	5.0	6.0 to 5.0		Low frequency background, semirhythmic	
14.0	5.0	2.0		Accelerating volleys every 15 sec.	
12.0	5.0	2.0 to 1.0		Accelerating volleys every 15 sec., partly synchronous with respiration	
12.5	5.0	1.5 to 0.0		Rhythm of 10 a sec for 1-2 sec. every 10-20 sec.	
12 5	5.0	—3.0		Sudden absence of background	
14.0	5.0	—6.0		Low frequency howl	
13.5	4.0	2.0		Volleys	
12.5	3.0	1.0		Sudden change in background	
13.5	1.5	11.0		Loud, rumbling, semirhythmic background suddenly appears	
12 0	1.5	6.0		Huge background	
13.5	1.5	3.0		Very loud background	
13.5	1.5	—5.0		Rhythm, 2-3 a sec., sharp and clicking	
14.0	1.0	2.0		Sudden increase in background	

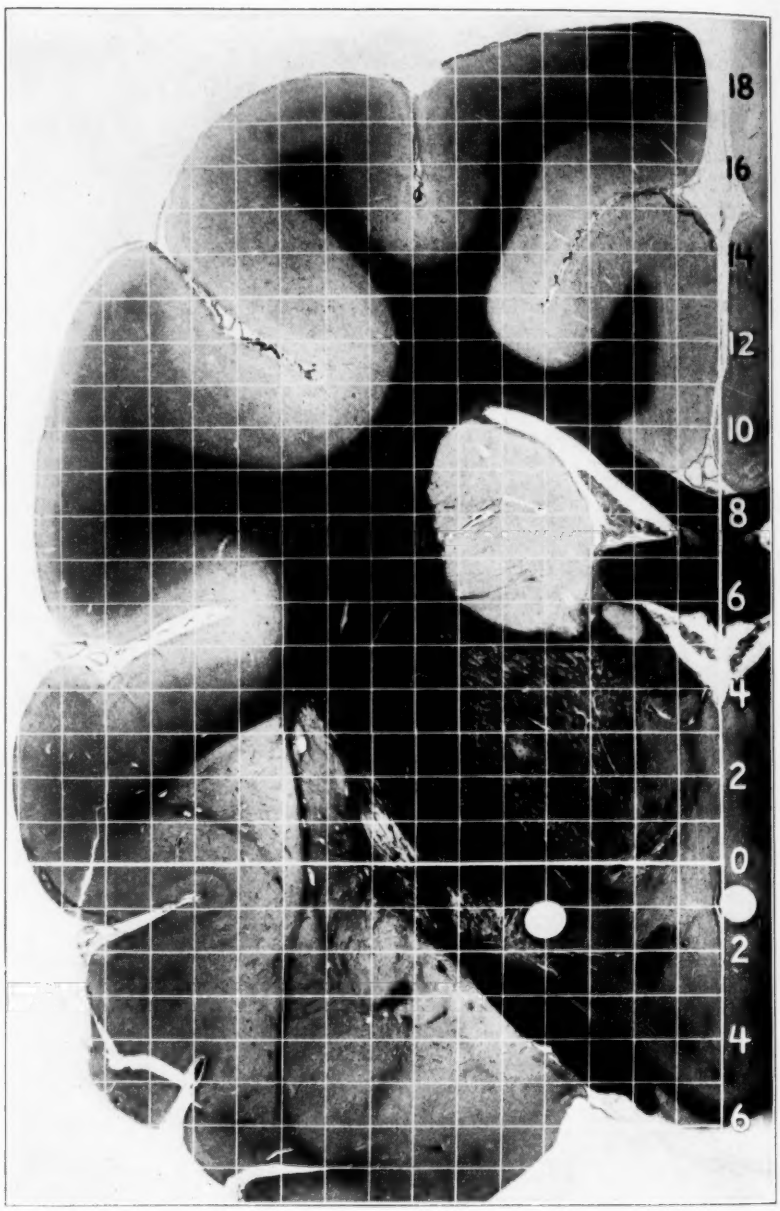

Fig. 8.—Photomicrograph of a section of the cat's brain in the frontal plane of the Horsley-Clarke instrument, 13.6 mm. in front of the interaural line.

TABLE 5.—*Data on Figure 9*

A	L	±	Structures	
10.8	15.0	13.0	Ectosylvian gyrus	
10.8	15.0	8.0	Anterior sylvian gyrus	
10.8	15.0	3.0	Acoustic radiations (lateral end)	
10.8	15.0	—0.5	Sylvian sulcus	
10.8	15.0	—4.0	Posterior sylvian gyrus	
10.8	12.0	2.0	Claustrum	
10.8	12.0	0.5	Extreme capsule	
10.8	12.0	—6.0	Posterior rhinal sulcus	
10.8	10.5	1.0	Putamen	
10.8	10.0	—4.0	Amygdala	
10.8	10.0	—7.0	Anterior commissure	
10.8	9.0	12.0	Suprasylvian sulcus	
10.8	9.0	6.0	Corona radiata	
10.8	9.0	1.0	Auditory radiations	
10.8	9.0	—2.5	Tail of caudate nucleus	
10.8	7.0	6.0	Reticular substance	
10.8	7.0	—3.0	Optic tract	
10.8	7.0	—5.0	Cornu ammonis	
10.8	6.0	15.0	Lateral sulcus	
10.8	6.0	9.0	Tail of caudate nucleus	
10.8	6.0	6.0	Dorsal part of lateral nucleus of thalamus	
10.8	6.0	1.0	Ventral part of lateral nucleus of thalamus	
10.8	6.0	—2.0	Internal capsule	
10.8	2.0	14.0	Splenic sulcus	
10.8	2.0	9.0	Callosum	
10.8	2.0	8.0	Fornix	
10.8	2.0	7.0	Dorsal portion of lateral nucleus of thalamus	
10.8	2.0	3.0	Medial nucleus of thalamus	
10.8	2.0	—1.0	Vicq d'Azyr's bundle	
10.8	2.0	—2.0	Hypothalamus	
10.8	2.0	—4.5	Descending portion of fornix	
10.8	1.0	3.0	Medial nucleus of thalamus	
10.8	0.5	12.0	Fornicate gyrus	
10.8	0.5	5.5	Taenia thalami	
10.8	0.0	3.0	Soft commissure	
			Auditory Responses	
10.0	12.0	S	Medium response	
			Somesthetic Responses	
10.8	12.0	5	Forepaws; high frequency volleys, faint	
10.8	10.0	7 to 5	Forepaws; high frequency volleys, strong	
10.8	8.0	7 to 3	Forepaws; high frequency volleys, strong	
10.8	7.0	—1	Response	
10.0	7.0	—1	Crossed hindleg and some from foreleg; flexion and extension	
10.0	6.5	1 to —1	Crossed foreleg, some from hindleg and trunk	
10.8	6.0	8	Crossed response to touch; volleys	
10.8	6.0	5	Jaws; discharges when open	
10.8	6.0	4 to 1	Crossed forepaw; volleys	
10.0	5.0	8	Crossed legs and abdomen; late slow wave after squeeze	
10.0	5.0	7	Crossed side	
10.0	5.0	4 to 0	Crossed foreleg and side; volleys for 3 sec. every 10 sec.; volleys altered by tactile stimulus	
10.0	5.0	1 to 0	Flexion or extension of crossed hindleg and toes gives burst at end of movement, also touch and pressure; crossed response greater than uncrossed, foot response greater than leg	
10.0	5.0	1 to 0	Crossed forepaw	
10.0	5.0	0 to —1	Footpads	
10.0	5.0	—1	Crossed foreleg only; response to blowing on fur and squeezing or bending toes	
10.0	5.0	—2	Crossed foreleg, some from hindleg	
10.0	4.5	—1	Body	
10.0	3.0	11 to 10	Uncrossed forepaws; squeeze	
10.0	3.0	—2	Uncrossed hindleg; flexion and extension	
10.0	3.0	—3	Crossed hindleg; flexion and extension	
			Optic Responses and Rhythms	
10.0	6.0	—7	Mild response	Faint rhythm
10.0	5.0	S	Response	Rhythm stopped by light in crossed eye
10.0	5.0	14	Response	Rhythm stopped by light in crossed eye
10.0	5.0	13	Response	Rhythm stopped by light in crossed eye
11.3	5.0	13	Response	—
10.8	5.0	13 to —5.5	—	Rhythm 3.2 a sec., made asynchronous with light; 4 a sec. with light off
9.8	5.0	12 to 7.9 M	—	Rhythm 3 a sec., with double beats; increased by crossed eye and stopped by uncrossed

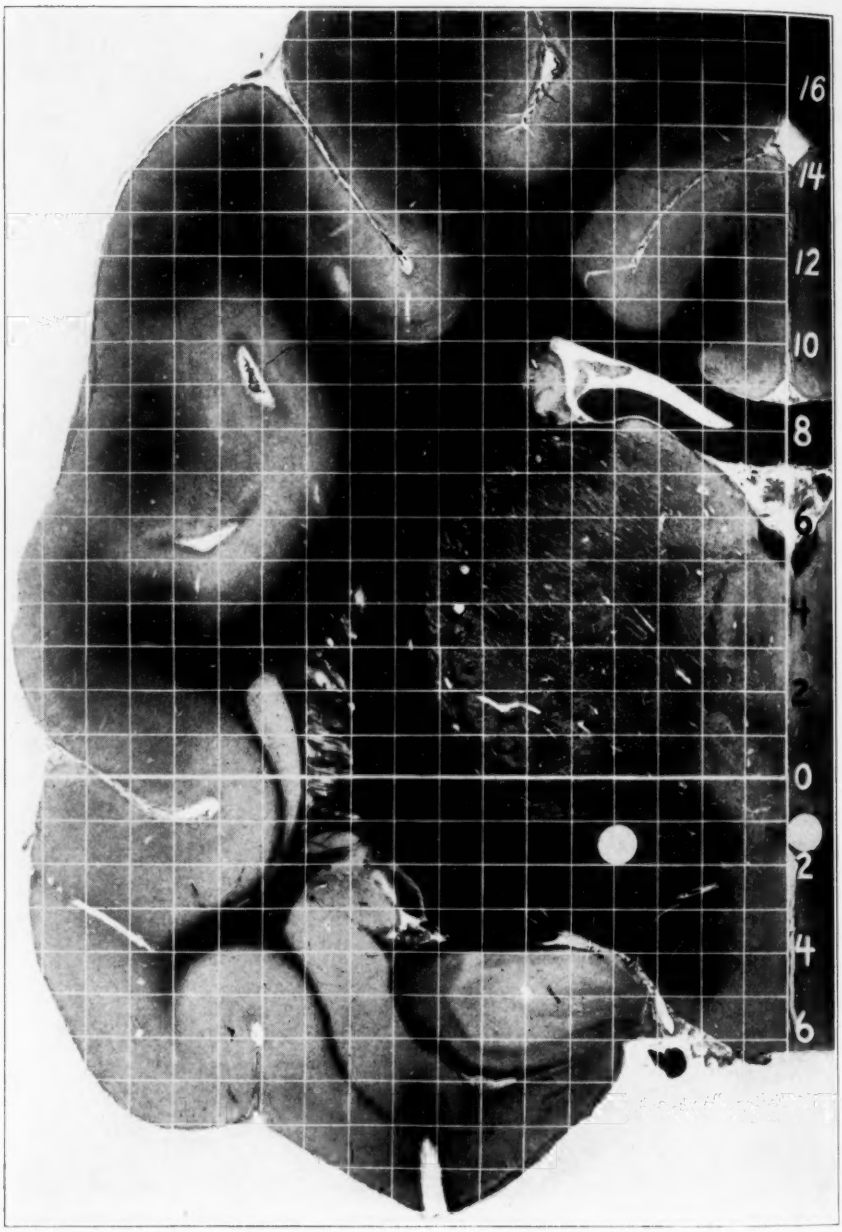

Fig. 9.—Photomicrograph of a section of the cat's brain in the frontal plane of the Horsley-Clarke instrument, 10.8 mm. in front of the interaural line.

TABLE 5.—*Data on Figure 9—Continued*

				Optic Responses and Rhythms—Continued	
11.3	5.0	4		Some crossed response	Rhythm
9.8	5.0	−2 to −4.0		—	Rhythm 3 a sec., stopped in 12 sec. by light in crossed eye
11.3	5.0	−3		Mainly crossed response; high pitched	Some rhythm
10.0	5.0	−3 to −4.0		Very strong response	—
11.3	5.0	−4		Huge response; sharp on and off, short after-discharge	Rhythm 2 a sec. for 20 sec. every few minutes; darkening uncrossed eye gives strong rhythm of 2.7 a sec., becoming 2.4 a sec., crossed eye, 2.6 a sec., both eyes, 2.7 a sec.; light in crossed eye makes rhythm asynchronous; in uncrossed eye makes background quiet but leaves rhythm at 2.4 a sec., which increases to 2.9 a sec. at once with light off; in light-adapted eye, rhythm at 3.5 a sec.; light on makes rhythm asynchronous, which increases to 4 a sec. after light
11.3	5.0	−5.0		Sharp response, gone at −5.5	—
10.8	5.0	−5.0		Huge response	Huge rhythm stopped mainly by crossed eye
10.8	4.0	−6.0 to −7		Strong response	Rhythm strong after dark adaptation
10.8	3.0	20.0 to 3		Response	—
9.8	3.0	18.0 to 15		Response	Irregular, chugging rhythm, stopped by light in both eyes
10.8	3.0	−1.0 to −5	M	High-pitched swishing response	—
10.0	3.0	−4.0 to −7		Response	—
10.8	3.0	−5.0 to −8		On and off response	—
11.3	3.0	−5.0 to −8		On and off response	—
11.3	3.0	−6.0		On only	Strong background
11.3	3.0	−6.5		On and off	Huge background
11.3	3.0	−7.0		Response	Rhythm 3.7 a sec., double; in and out of phase every 3-4 sec.; increased with dark adaptation; crossed eye (slit pupil) stops rhythm, uncrossed (dilated pupil) increases rhythm or makes it asynchronous; both give moderate inhibition; later, with light-adapted eyes after atropine, rhythm 3.2 a sec., crossed eye stops, uncrossed eye increases it or has no effect
11.3	3.0	−7.5 to −9		On and off response	Background stopped by light
10.0	2.0	−6.0		Response	Rhythm not stopped by light
10.0	2.0	−7.0		Response	Regular rhythm 2.2 a sec.
10.8	0.0	−6.0		Response	—
				Spontaneous Activity	
10.7	6.0	0.0 to −5		Howl	
10.0	5.0	20.0 to 15		Needle movement down to +15 gives deep-pitched roaring discharge	
10.0	5.0	7.5		Loud roar, suddenly out	
10.0	5.0	5.0		Rhythm of 3 a sec. at 20 sec. intervals	
10.0	5.0	1.0 to 0		Volleys every 10 sec.	
10.0	4.0	6.0 to 2		Accelerating volleys every 15 sec.; loud steady background at lower edge	
11.3	3.0	4.5 to −2		Double rhythm and volleys 3 a sec.; background changes at 0	
10.0	3.0	12.0		Rhythm, 50 a sec.	
10.7	3.0	10.0 to 9		Loud "hollow," low-pitched background in this millimeter	
10.7	3.0	5.0		Rhythm, 8 a sec.	
11.3	1.5	5.0		Sudden background; struggles as needle advances to 0	

Experiments already referred to have demonstrated a marked effect of potassium and calcium ions on the electrical activity of the brain, as well as on motor discharges. The postural after-discharge of cerebellar stimulation is increased by increased potassium in the blood and is decreased by increased calcium (Gerard and Magoun [51]), and effects of carbon dioxide, reported in this paper, have also been shown to modify the brain rhythms in human subjects.

We hope further to obtain rhythms in isolated nerve cells or masses and to study the effect of these various agents on them. The brain of the chick embryo has proved inactive until hatching, but the isolated frog cerebrum gives potentials. Cultures of adult nerve cells may yield results with micro-electrodes.

SUMMARY

Electrical activity spontaneously present, as well as that evoked by auditory, somesthetic, optic and other stimuli, has been explored in the cat's encephalon from the inferior colliculus forward.

Sharply localized potentials were picked up with a concentric electrode guided by the Horsley-Clarke instrument, fed into a resistance-capacity-coupled amplifier and observed on the cathode ray oscillograph and from the loud-speaker. The brain was exposed widely or through fine drill holes, with the subject under light anesthesia induced with tribromethanol or pentobarbital sodium, supplemented when needed with ether.

The bulk of the findings are summarized in relation to ten photomicrographs of coronal brain sections in the frontal plane of the Horsley-Clarke instrument, which serve to correlate anatomic structures and electrical activity.

Additional information is given in the text as to thresholds (often at about the level in man), periods of latency, shapes of waves, locations of action potentials in response to sensory stimuli, rhythmic or irregular spontaneous potential waves, and the influence of optic and other stimuli on them. The relation of the number and organization of active neural elements to the form and magnitude of the recorded potentials is considered.

Responses to the modalities of stimuli used were followed through recognized tracts and nuclei to the cortical surface and were localized in the whole projection fields, or even more finely—as in the case of proprioceptive impulses from varying regions of the body.

As impulses pass centrally there is considerable interaction between those in separate elements of one sensory system, or even between those of separate systems (optic and auditory).

---

51. Gerard, R. W., and Magoun, H. W.: Proc. Soc. Exper. Biol. & Med. **34**: 755, 1936.

TABLE 6.—*Data for Figure 10*

A	L	±		Structures
7.9	16.0	7.0		Posterior sylvian gyrus
7.9	16.0	—3.0		Posterior ectosylvian sulcus
7.9	14.0	14.0		Ectosylvian gyrus
7.9	14.0	—7.0		Posterior ectosylvian gyrus
7.9	12.0	4.0		Sagittal fiber layers
7.9	12.0	—7.0		Posterior rhinal sulcus
7.9	11.0	2.0		Tail of caudate nucleus
7.9	10.0	11.0		Suprasylvian sulcus
7.9	10.0	6.0		Beginning of optic radiations
7.9	10.0	4.0		Dorsal nucleus of lateral geniculate body
7.9	10.0	3.0		Ventral nucleus of lateral geniculate body
7.9	10.0	1.0		Optic tract
7.9	10.0	—1.0		Stria semicircularis
7.9	10.0	—4.0		Cornu ammonis
7.9	8.0	—2.0		Anterior end of medial geniculate body
7.9	7.0	8.5		Tail of caudate nucleus
7.9	7.0	7.0		Beginning of optic radiations
7.9	7.0	2.0		Ventrolateral nucleus of thalamus
7.9	7.0	—1.5		Acoustic radiations
7.9	5.0	7.0		Pulvinar (dorsal nucleus of thalamus)
7.9	5.0	—1.0		Hypothalamus
7.9	5.0	—4.0		Cerebral peduncle
7.9	3.0	18.0		Lateral gyrus
7.9	3.0	12.0		Splenial sulcus
7.9	3.0	2.0		Central nucleus of thalamus
7.9	1.5	—4.0		Peduncle of mamillary body
7.9	1.0	16.0		Splenial gyrus
7.9	1.0	4.0		Habenular nucleus
7.9	1.0	2.0		Meynert's tract
				Auditory Responses
8.0	12.0	S to 3.8 M		Response
8.0	12.0	—1.5 to —2.5		Auditory response increased by optic response
8.0	8.0	0.0 to —3.0	0.5 M	Response
				Somesthetic Responses
8.0	8.0	2.0		Squeezing hindleg stops volleys otherwise present
8.0	8.0	2.0 to 1		Crossed foreleg
8.0	8.0	2.0 to 0		Crossed foreleg and hindleg; strong touch response
8.0	8.0	1.5		Crossed foreleg; stroking fur
7.0	8.0	22.0 S		Abdomen, back; touch
7.0	8.0	14.0		Strong touch
8.0	8.0	2.0		Squeeze of hindleg stops volleys otherwise present
8.0	8.0	2.0 to 1		Crossed foreleg
8.0	8.0	2.0 to 0		Crossed foreleg and hindleg; strong touch
8.0	8.0	1.5		Crossed foreleg; stroking fur
8.0	7.0	2.5 to 0		Crossed foreleg and hindleg; good response to touch of one hair, below human threshold
9.0	7.0	1.5 to 0		Crossed forepaw and leg, some from uncrossed leg; very strong touch response; roaring background
8.0	6.5	2.5 to 0		Response
8.0	6.5	—1.0		Crossed foreankle; bending, none to touch
8.0	6.0	14.0		General touch
8.0	5.0	8.0		Stroking body fur
8.4	5.0	3.0 to 0		Crossed foreleg, some from hindleg and body; foreleg response huge; responses reversed at 5 mm. to right of midline
8.0	5.0	3.0 to 0		Crossed foreleg very strong, also hindleg and body; touch
9.0	5.0	2.0 to 0		Crossed forepaw and leg, some from uncrossed leg
8.4	5.0	0.0		Crossed forepaw; bending
8.0	5.0	0.0 to —1		Crossed foreleg, little from paw; touch and bending
8.0	5.0	0.0 to —2		Crossed foreleg and some from hindleg; touch below knees; squeezing toes
8.0	5.0	—1.0		Crossed foreleg and paw; stroking and pressure
8.0	5.0	—2.0		Maintained discharge and off burst to squeezing or stretching of crossed foreleg
8.0	4.0	15.0		General touch
8.0	4.0	6.0		Stroking fur on back
8.0	4.0	5.0		Strong; uncrossed leg
8.0	4.0	4.0		All paws; bending
8.0	4.0	0.0		Bursts every 20 sec. with fur roughed forward
8.0	3.0	8.0		Crossed chest; tactile
8.0	3.0	4.0		Crossed chest and abdomen; tactile
8.4	3.0	0.0		Crossed forepaw; bending
8.0	3.0	0.0 to —2		Crossed forepaw; squeezing or stretching
8.0	3.0	—2.5		Foreleg and foot
9.0	1.0	3.5 to 1		Blowing against head
				Optic Responses and Rhythms
8.0	12.0	6.0 to —6	—3 M	Crossed greater than uncrossed; suddenly less below —3 —
8.0	10.0	18.0 to 9		Response —

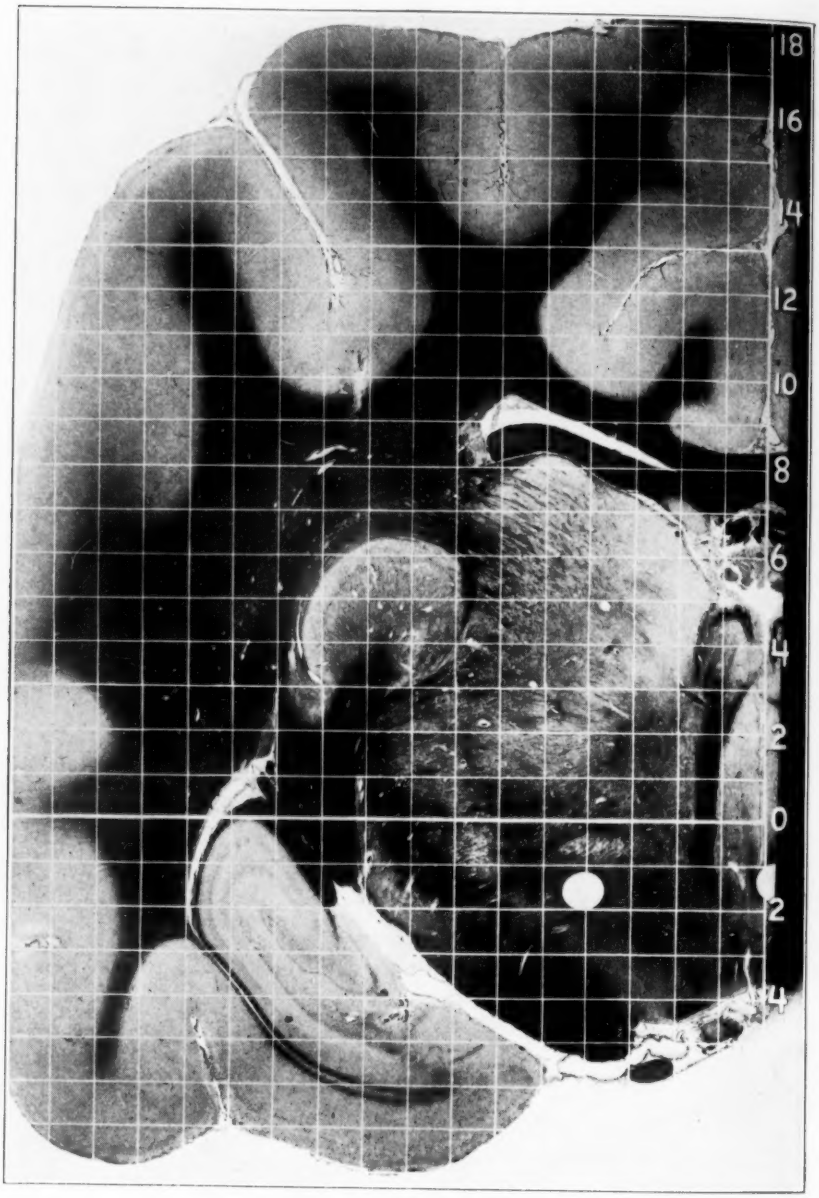

Fig. 10.—Photomicrograph of a section of the cat's brain in the frontal plane of the Horsley-Clarke instrument, 7.9 mm. in front of the interaural line.

TABLE 6.—*Data for Figure 10—Continued*

A	L	±	Structures	
8.0	10.0	7.0 to −3 +3 M	Response very strong and continuous and long after discharge; standing wave with constant stimulation	—
8.0	10.0	6.0	—	Good rhythm 4 a sec.; double; shows beats and waxes and wanes with blurring owing to asynchrony; stopped by light, returns stronger, sharper and sometimes faster in dark; 1 hr. later takes 1-5 sec. to return in dark
8.0	10.0	5.0	—	Rhythm
8.0	9.5	7.0	—	Rhythm 2.2 a sec., stopped by light
8.0	9.0	5.0	Slight response	Slight rhythm
8.0	9.0	3.0	After-discharge of 6 sec. after light on for 15 sec.	Rhythm 2.2 a sec. stopped by light; double beats with light; later 2.6 a sec., stopped by light but returns at 2.3 a sec.
8.0	10.0	5.0	—	Rhythm
8.0	9.5	7.0	—	Rhythm 2.2 a sec., stopped by light
8.0	9.0	2.0	Slight response; after-discharge lasts over 2 min.	Slight rhythm
8.0	8.0	19.0 S to 1	Huge response at 3; sharp on and off and long after-discharge	—
8.0	8.0	12.5	Faint on and off responses	—
8.0	8.0	11.0	—	Rhythm waxes and wanes over 20 beats
8.0	8.0	9.0 to 1 5 M	Response	Rhythm 0.5-1 a sec.
8.0	8.0	8.0	Crossed on response and uncrossed on and off give 1-3 distinct bursts	Rhythm fairly regular in dark, 1 a sec., semiregular in room light; stopped by light in eyes
8.0	8.0	7.0 to 1	Long after-discharge at 1	—
8.0	8.0	7.0	Marked on and off response	Rhythm, 10-20 volleys at 4 a sec.
8.0	8.0	5.0	Strong response; definite on and off response to forceps movement	Rhythm, 6 a sec., double; stopped then increased by light
8.0	8.0	5.0 to 1 M	Strong response; definite response to distant finger movement	Rhythm strong at 3; waxes and wanes 3 times a sec.; stopped by light
8.0	8.0	−3.0 to −6	Crossed response much greater than uncrossed	—
8.0	7.0	−6.0	Crossed response only	—
8.0	6.0	20.0 S to 12 14 M	On and off discharge at high frequency	—
8.0	6.0	−5.0	Faint response	—
7.8	5.0	21.0 S	Response; faint at surface	—
7.8	5.0	15.0 to 14	Response	Rhythm 3.3 a sec.; made irregular by crossed eye; uncrossed eye gives brief inhibition, then increases to 4 a sec.
8.4	5.0	15.0 to 12 13 M	Crossed and uncrossed responses equal; harsh irregular volleys; long after-discharge	Rhythm 4 a sec.; stopped only by crossed eye
9.2	5.0	14.0	Response	Rhythm stopped by crossed eye, increased by uncrossed
9.2	5.0	−3.0	Crossed and uncrossed responses; very high frequency	—
7.8	3.0	21.0 S to 19 M	On and off responses in both eyes	Double rhythm stopped only by crossed eye
9.2	3.0	21 0 to 15 18 M	Uncrossed on response	Rhythm stopped by crossed eye
8.4	3.0	20.0 S to 13	Response	Double rhythm stopped only by crossed eye
8.0	3.0	12.0	—	Rhythm 3 a sec., stopped by light
9.0	1.0	−2.0	Slight response	—
			Spontaneous Activity	
8	12.0	8.0 to 3	Loud background	
8	12 0	−7.0	Rhythm 10 a sec.	
8	10.0	5 0	Background	
8	10.0	2 0	Huge background; semirhythmic	
9	9.5	11 0	Musical note in background	
9	9.5	10 0 to 3	Volleys	
9	9.5	2.0	Very strong background	
8	9.0	9 0 to 0	Volley of 7 discharges every 5 sec.	
8	8.5	15 S	Irregular rhythm and volleys every 5 sec.; large bursts with leg movements	
8	8.0	13.5	Rhythm waxes and wanes in 4 sec. pulses	
8	8.0	9.0 to −1 3 M	Volleys and steady background; rhythm for 4 sec. every 30 sec.	
8	8.0	5.0 to 2	Howls suddenly at 5	
8	8 0	4.0	Volleys and steady background	
8	8.0	2.0	Volleys stopped by squeezing hindleg	
9	1.0	−4.5	Traction of liver repeatedly gives strong bursts which become a rhythm of 3 a sec., lasting from 5 to 30 sec.	

A rhythm of from 2 to 4 a second is commonly present throughout the optic structures, from the chiasm to the striate cortex. This is usually disrupted by visual stimuli, but is sometimes enhanced; occasionally illumination of each eye separately produces one of these opposed effects. Other spontaneous rhythms associated with the heart beat or respiration were highly localized; intense, though often irregular, activity was the rule in the main afferent and efferent systems and in the gray masses of the brain stem.

The action of anesthetics, carbon dioxide, etc., on potentials is reported.

The question of mass action is discussed in relation to localization of through connections and to interaction of impulses and synchronized cellular activity. It is concluded that individual neurons possess a potential rhythmicity and automaticity, which lead to "beating," and that cell groups are normally unified by a "distance action," in addition to conducted impulses. The latter impulses surely serve for more distant integrations, such as those in the subordination of lower to higher centers, as well as to shift an existing equilibrium pattern on sensory stimulation. The ultimate control of neuronal rhythmicity resides in the physicochemical properties of the cell, as determined (perhaps with a qualitative local specificity) by those of the bathing fluids.

APPENDIX.—The following plates and tables represent ten coronal planes of the cat's brain from 16 mm. anterior to 4 mm. posterior to the interaural plane. The median sagittal and zero horizontal planes are indicated on each photomicrograph, and a grid divides the plate into millimeters, which serves to locate any structure in terms of its Horsley-Clarke coordinates.

Corresponding to each plate is a table of structures and electrical activities in or near the plane of the plate. These are grouped under: anatomic structures, auditory responses, somesthetic responses, optic responses and rhythms and spontaneous activity, in the order given. Observations under each rubric are listed in order from the more lateral to the more medial positions and, for each lateral position, from above downward. Since the movement of the needle was in the vertical plane, the last coordinate often gives both the point of appearance and that of disappearance of the phenomenon in question. The coordinates are expressed in millimeters: A indicates anterior to, and P, posterior to, the interaural plane; L, distances lateral to the median sagittal plane, and + and —, distances above and below the zero horizontal plane. Other symbols used are: S, indicating an observation made on the cortical surface before penetration of the needle, and M, maximum intensity.

It is to be noted that many routine observations are omitted, so that points not listed were not electrically dead. But all observations in any way unique are included. When more than one observation is listed for a given point or for overlapping vertical stretches, each is for a different cat.

It should be emphasized again that the Horsley-Clarke coordinates permit localization only to a first approximation of 1 or 2 mm. This atlas may be used to locate only grosser structures with confidence. The finer analysis of small nuclei and tracts, as in the work of Ranson's laboratory, depends on a direct histologic check.

TABLE 7.—*Data for Figure 11*

A	L	±	Structures	
6	15.0	12.0	Ectosylvian gyrus	
6	15.0	8.5	Ectosylvian sulcus	
6	15.0	4.0	Posterior sylvian gyrus	
6	15.0	0.0	Posterior ectosylvian sulcus	
6	15.0	—5.0	Posterior ectosylvian gyrus	
6	12.0	5.0	Sagittal fiber layers	
6	12.0	0.0	Cornu ammonis	
6	8.0	8.0	Tail of caudate nucleus	
6	8.0	5.0	Lateral geniculate nucleus	
6	8.0	2.0	Medial geniculate nucleus	
6	8.0	—1.0	Lateral lemniscus	
6	6.0	10.0	Subcallosal stratum	
6	5.0	9.0	Alveus	
6	5.0	6.0	Pulvinar (dorsal nucleus of thalamus)	
6	5.0	0.0	Ventral nucleus of thalamus	
6	5.0	—2.0	Hypothalamus	
6	5.0	—3.0	Substantia nigra	
6	5.0	—5.0	Cerebral peduncle	
6	3.0	8.0	Fascia dentata	
6	2.0	3.0	Superior colliculus	
6	2.0	—4.0	Vicq d'Azyr's bundle	
6	1.0	8.0	Splenium of corpus callosum	
6	1.0	1.0	Posterior commissure	
6	1.0	—3.0	Guddens tract	
6	0.0	1.0	Aqueduct of Sylvius	
6	0.0	0.0	Central gray substance	
6	0.0	—3.0	Forel's decussation	
			Auditory Responses	
6	10.0	9 to 8	Tick gives moderate response	
5	8.5	1 to —1	Response	
			Somesthetic Responses	
6.0	10.0	8.0 to 4.0	General sensory; volleys	
6.2	8.5	S	All legs; bending	
7.0	8.0	22.0 S	Abdomen and back; touch	
7.0	8.0	14.0	Strong touch response	
6.0	8.0	4.0 to 1.0	Crossed forepaw; volleys	
7.0	7.0	2.0 to 0.0	Crossed forepaw only; touch response very strong	
6.0	6.0	2.0 to 1.0	Crossed forepaw; volleys	
6.2	5.5	21.0 S to 13.0	Abdomen and back; strong touch response	
6.2	5.5	1.0 to —1.0	Crossed forepaw strong, other crossed regions feeble; touch	
6.2	5.0	1.5 to —1.5	Crossed forepaw only	
7.0	5.0	0.0 to —1.0	Crossed forepaw only	
7.0	5.0	0.0 to —2.0	Crossed forepaw only	
6.2	3.0	2.0 to —1.0	Crossed forepaw only	
			Optic Responses and Rhythms	
6.0	8.0	5.0	Faint response	Faint rhythm; deep anesthesia
6.0	6.0	8.0 to 7	Response	—
6.0	6.0	—5.0	Huge response with delayed on and off, followed by long after-discharge	Roaring discharge after turning light off; fades in 2 min. to faint rhythm
7.0	5.0	21.0 S	Response	Rhythm stopped by crossed eye
6.0	5.0	21.0 to 12	Response	Rhythm stopped by crossed eye
7.0	5.0	14.0 M to 12	Very strong response; disappears sharply at 12	—
6.0	4.0	17.0 S	Response	—
6.0	4.0	15.0 S to 10	Strong response	Rhythm clear and double in dark-adapted eye; one is continuous at 2.7 a sec.; the other comes and goes in volleys at 3 a sec.
6.0	4.0	14.5	Response	—
6.0	4.0	10.0	Response	Rhythm 3 a sec.
6.0	4.0	—5.0	Strong on, weak off response	—
6.0	4.0	—6.5 to —8	On and off response	Terrific roar in dark, stopped by light; with light off roar returns for 30 sec., then quiets to faint double rhythm; during needle penetration both eyes first dilate and then constrict; then crossed eye constricts and uncrossed eye dilates
7.0	3.0	21.0 to 15	Double response at on and off	Rhythm
6.0	3.0	20.0 S to 12 19 M	Response	Rhythm stopped by crossed eye
6.0	2.0	17.0 to 11 14 M	Strong response	Rhythm clear and double in dark-adapted eye; one is continuous at 2.7 a sec., the other comes and goes in volleys at 3 a sec.
			Spontaneous Activity	
7.0	7.0	—5	From 7-10 accelerating discharges every 7 sec.	
6.2	5.0	—4	Volleys on a quiet background	
6.2	3.0	—4	Volleys on a quiet background	

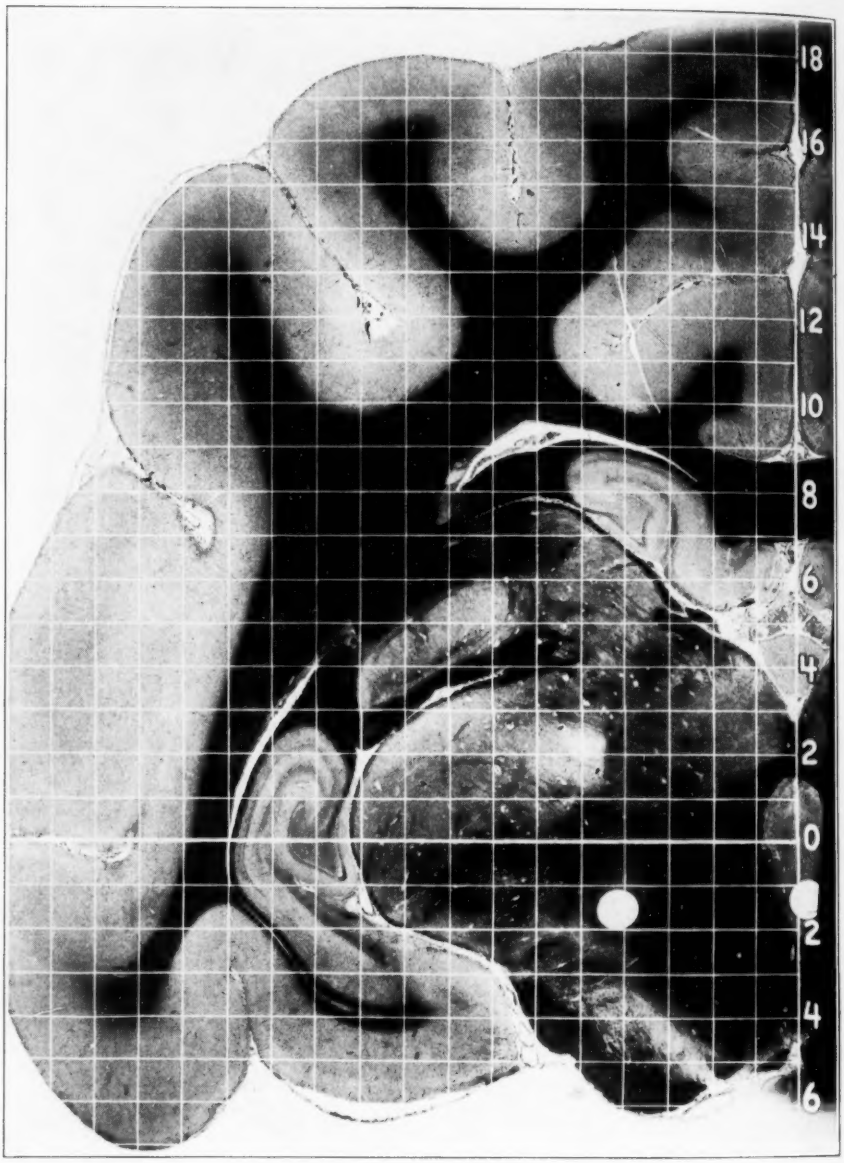

Fig. 11.—Photomicrograph of a section of the cat's brain in the frontal plane of the Horsley-Clarke instrument, 6 mm. in front of the interaural line.

TABLE 8.—*Data for Figure 12*

A	L	±			Structures	
4	15.0	6.0			Posterior suprasylvian gyrus	
4	15.0	—4.0			Ectosylvian gyrus	
4	12.0	15.0			Suprasylvian sulcus	
4	12.0	4.0			Sagittal layers of radiations	
4	12.0	—3.0			Posterior rhinal sulcus	
4	9.0	17.0			Suprasylvian gyrus	
4	9.0	4.0			Cornu ammonis	
4	9.0	—3.0			Pyriform lobe	
4	7.0	1.0			Medial geniculate nucleus	
4	6.0	0.0			Brachium of inferior colliculus	
4	5.0	—3.0			Lateral lemniscus	
4	4.0	18.0			Lateral gyrus	
4	4.0	13.0			Splenial gyrus	
4	4.0	—1.0			Tegmentum	
4	4.0	—5.0			Substantia nigra	
4	4.0	—6.0			Cerebral peduncle	
4	3.5	—4.5			Medial lemniscus	
4	2.0	16.0			Suprasplenial gyrus	
4	2.0	4.0			Superior colliculus	
4	2.0	2.0			Posterior commissure	
4	2.0	—2.0			Tegmentum	
4	2.0	—3.0			Red nucleus	
4	0.5	1.0			Central gray substance	
4	0.5	—2.0			Oculomotor nucleus	
					Auditory Responses	
4	8.0	2.0 to 1			Response increased by light	
					Somesthetic Responses	
4	8.0	0.0			Crossed foreleg response	
					Optic Responses and Rhythms	
3	11.0	1.5			Very strong response; sharp on and off	—
4	8.0	14.0 to	0	6 M	Sharp on and off	Marked rhythm best at 14 and 2
4	8.0	13.0 to	9		Coarse response	—
4	8.0	6.0 to	3		Response	Rhythm
4	8.0	6.0 to	2		Response	Rhythm
4	8.0	7.0 to	2		Crossed response strong and continuous	—
3	8.0	4.0 to	2	3 M	Very strong response	—
4	8.0	3.0 to	2		Response	—
4	8.0	3.0			—	Rhythm for 3 sec. every 10 sec.
4	8.0	—4.0 to	—6		Response	"Standing locomotive" rhythm and loud background
4	4.0	14.5 to	11		Coarse, sharply localized response	—
3	4.0	14.0			Response	—
4	3.0	4.5			Off response only	—
					Spontaneous Activity	
4	8.0	13.0			Volleys every 10 sec.	
4	8.0	6.0			Regular accelerating volleys, becoming intermittent on illumination	
4	8.0	0.0			Loud background	
4	4.0	—2.5			Very strong background	
4	4.0	—5.0			Rhythm synchronous with respiration	
4	3.0	—1.0			Sharp change in background	
4	3.0	—3.0			Rhythm 100 a sec. on placing needle and for several minutes longer	
4	3.0	—4.5			Sudden decrease in background	
3	2.0	0.0			Howls	
4	0.0	—5.0			Huge background, which fades in 1 min.	

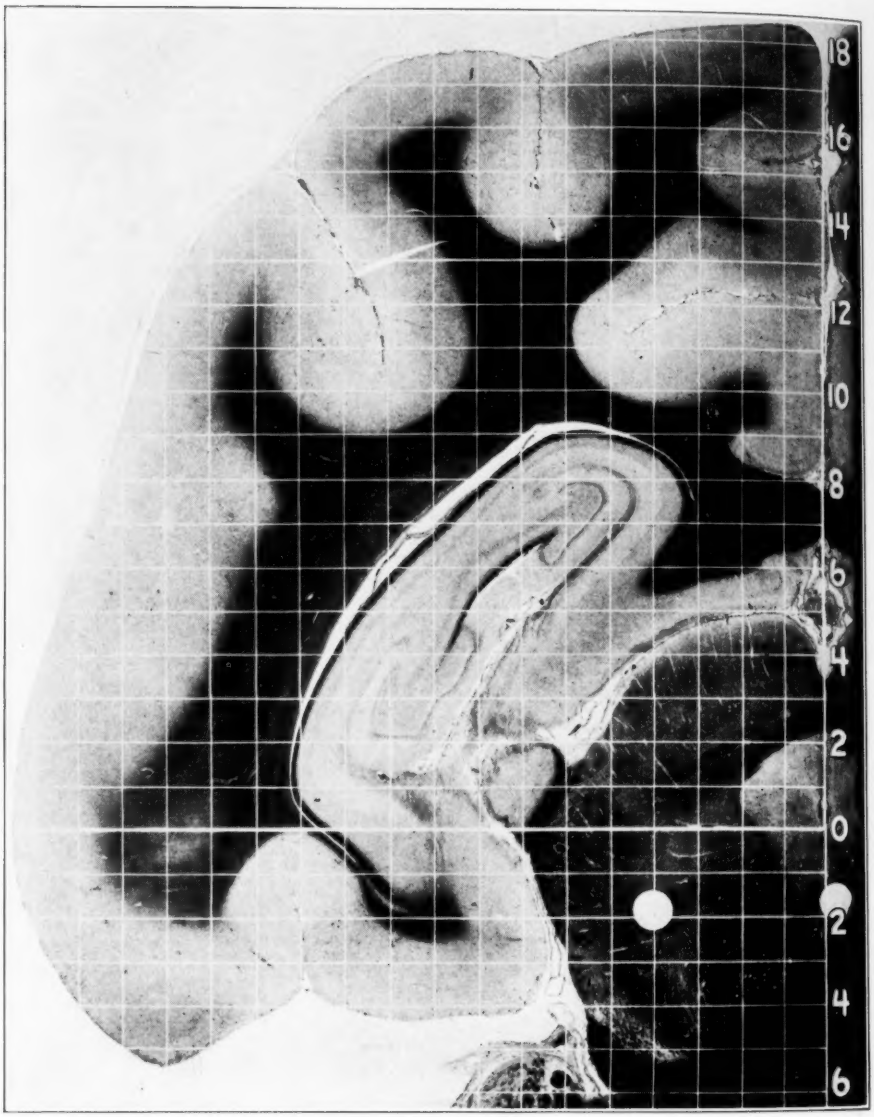

Fig. 12.—Photomicrograph of a section of the cat's brain in the frontal plane of the Horsley-Clarke instrument, 4 mm. in front of the interaural line.

TABLE 9.—*Data for Figure 13*

A	L	±	Structures	
2	16.0	7	Posterior ectosylvian gyrus	
2	8.0	6	Cornu ammonis	
2	6.0	0	Brachium of inferior colliculus	
2	4.0	1	Deep medullary stratum of superior colliculus	
2	4.0	—4	Cerebral peduncle	
2	3.0	4	Superior colliculus	
2	3.0	—1	Reticular substance of tegmentum	
2	2.0	—3	Red nucleus	
2	1.0	1	Central gray matter	
2	0.5	—2	Oculomotor nucleus	
			Auditory Responses	
2	8.0	0	Faint response	
2	6.0	—1	Response to tuning fork or voice as fine standing waves, changing with pitch; strong response to metronome beats	
			Optic Responses and Rhythms	
2	10.0	15 to 6 14 M	On and off responses each show 4 distinct waves; crossed greater than uncrossed	—
2	10.0	3 to 2	On and off responses	"Standing locomotive" rhythm every 5 sec.
2	8.0	S to 8	High frequency, even response	Rhythm very regular at 1.7 a sec.; later 1.5 a sec., double and with beats; stopped by light but returning after few seconds in dark; no activity in lighted room; darkening both eyes elicits a roar and a rhythm in 3-4 sec., and either eye a roar, becoming rhythmic in 7 sec.
2	8.0	18 to 15	On and off responses	—
2	8.0	8	Strong response	Strong rhythm stopped by crossed eye
2	8.0	6 to 2 4 M	High frequency, continuous discharge with light; off short at 4 and long at 3	Rhythm very regular, 1.7 a sec.; later 1.5 a sec., double and with beats; stopped by light but returning after few sec. in dark
2	8.0	6 to 2	On response and continuous discharge with light	Rhythm 3 a sec. after light on
2	8.0	—3	On and off responses	—
2	6.0	20 to 18	Response	Rhythm
2	6.0	5	Response	Rhythm
2	4.0	S and below	Response	Rhythm 1.3 a sec. with dark adaptation; light changes rate
			Spontaneous Activity	
2	8.0	—4	Sudden decrease in background	
2	4.0	10	Large, slow potentials	
2	2.0	1	Musical note as background	
2	2.0	—1 to —3	Roar	

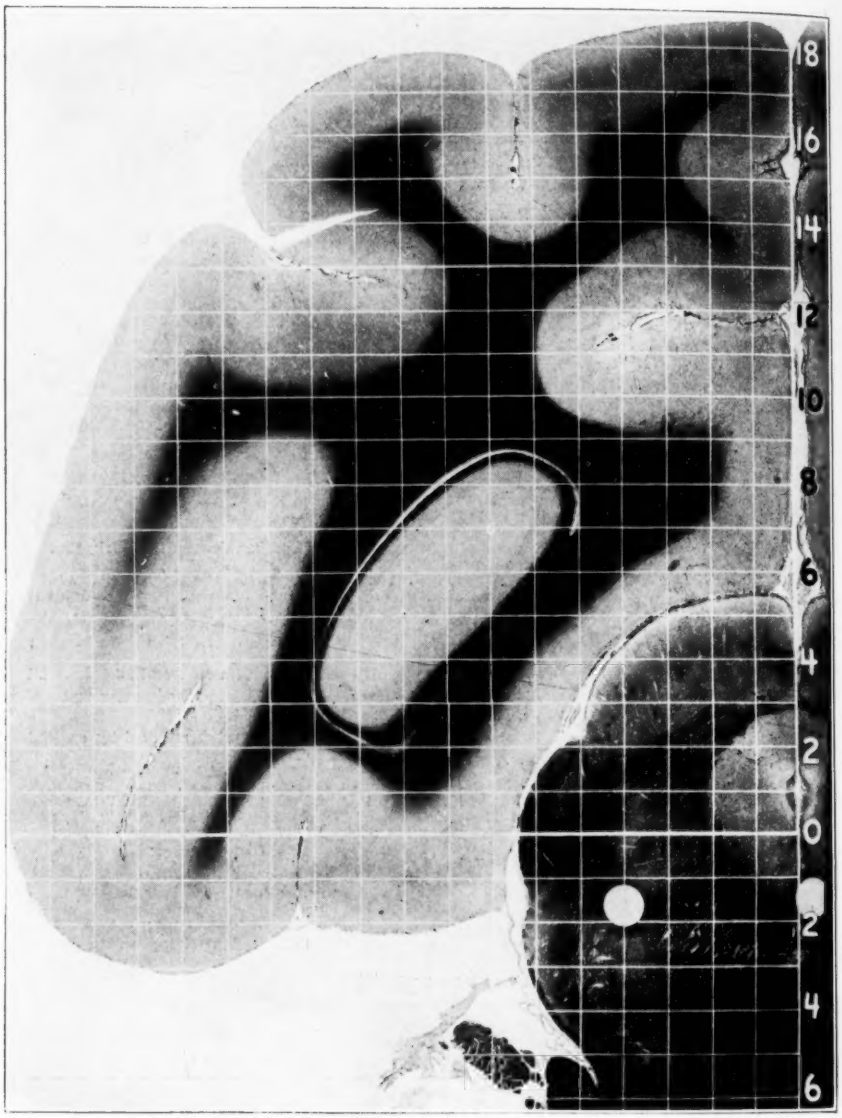

Fig. 13.—Photomicrograph of a section of the cat's brain in the frontal plane of the Horsley-Clarke instrument, 2 mm. in front of the interaural line.

TABLE 10.—*Data for Figure 14*

A	L	±		Structures	
0.2	11.0	15.0		Suprasylvian gyrus	
0.2	11.0	13.0		Suprasylvian sulcus	
0.2	7.0	10.0		Sagittal layers of radiations	
0.2	7.0	5.0		Fornicate gyrus	
0.2	6.0	16.0		Lateral sulcus	
0.2	6.0	—4.0		Brachium pontis	
0.2	5.0	16.0		Lateral gyrus	
0.2	5.0	3.0		Inferior colliculus	
0.2	5.0	—2.0		Lateral lemniscus	
0.2	4.0	17.0		Lateral sulcus	
0.2	4.0	—3.0		Reticular substance	
0.2	4.0	—6.0		Corticopontile parapyramidal fibers	
0.2	4.0	—7.0		Pontile nuclei	
0.2	3.0	—3.0		Superior cerebellar brachium	
0.2	3.0	—7.0		Pyramidal fibers	
0.2	2.0	17.0		Lateral gyrus	
0.2	2.0	4.0		Superior colliculus	
0.2	2.0	1.0		Mesencephalic tract of fifth nerve	
0.2	2.0	—1.5		Posterior longitudinal bundle	
0.2	2.0	—5.5		Medial lemniscus	
0.2	1.5	—0.5		Trochlear nucleus	
0.2	1.5	—2.0		Posterior longitudinal bundle	
0.2	1.0	0.0		Central gray substance	
0.2	1.0	—4.0		Predorsal bundle	
0.2	0.0	—3.0		Meynert's decussation	
0.2	0.0	—5.0		Interpeduncular ganglion	
				Auditory Responses	
0	14.0	S to 14	M	Marked response to tick	
0	12.0	S		Moderate response to tick	
0	12.0	3.0 to 0	M	Sharp response to tick	
0	10.0	S		Moderate response to tick	
0	10.0	2.0		Moderate response to tick	
0	10.0	—1.0		Moderate response to tick	
0	10.0	—1.5		Response to voice but not to tick	
0	8.0	4.0 to —6	—2 M	Response to tick	
0	8.0	4.0 to —2	0 M	Response to tick	
0	8.0	3.0 to —3	0 M	Response to tick	
0	8.0	1.5 to —1		Response to tick	
0	6.0	4.0 to —6	—1 M	Response to tick	
0	6.0	—1.0		Standing waves with fork and voice; response to metronome	
0	6.0	—3.0		Response to tick	
0	6.0	—4.0		Faint response	
0	4.0	S to 14		Response to tick	
0	4.0	18 0 to 15	15 M	Response to tick	
0	4.0	5.0		Faint response to tick	
0	4.0	4.0 to —8	0 M	Response to tick	
0	4.0	2.0		Strong response to tick	
0	4.0	2.0 to —2		Response to tick	
0	4.0	—3.0		Response to tick	
0	2.0	3.0 to —2		Response to tick	
				Somesthetic Responses	
0	8.0	—1.0 to —5		Crossed hindpaw strong, forepaw feeble (auditory impulses and heart rhythm also present)	
0	6.0	1.5		Both forelegs and chest	
0	6.0	0.5		Paws only	
0	6.0	—1.0		Crossed forepaw	
0	6.0	—1.0 to —2.5		Crossed forepaw	
0	4.0	1.0		Crossed forepaw; rhythm, not affected by cutaneous stimulation	
0	4.0	—2.0		Crossed forepaw strongest, but all others present; touch and bending; definite on and off as well as sustained discharge; rhythm 2.3 a sec.	
0	4.0	—4.0		General cutaneous; rhythm	
0	2.0	—6.0		General cutaneous; crossed stronger	
				Optic Responses and Rhythms	
0	14.0	4.0		Good after-discharge	Good rhythm 4 a sec., stopped by light
0	12.0	9.0 to 5.0		Strong, mainly crossed response; sharp on and continuous course, growling discharge	—
0	12.0	9.0 to 0.0	3.5M	Response, almost gone at 6	—
0	12.0	8.0		Response	Rhythm 4 a sec., stopped by light
0	12.0	5.0 to 3.0		Response	—
0	12.0	2.4		—	Huge background; some rhythm 3 a sec.; stronger and faster with light in crossed eye

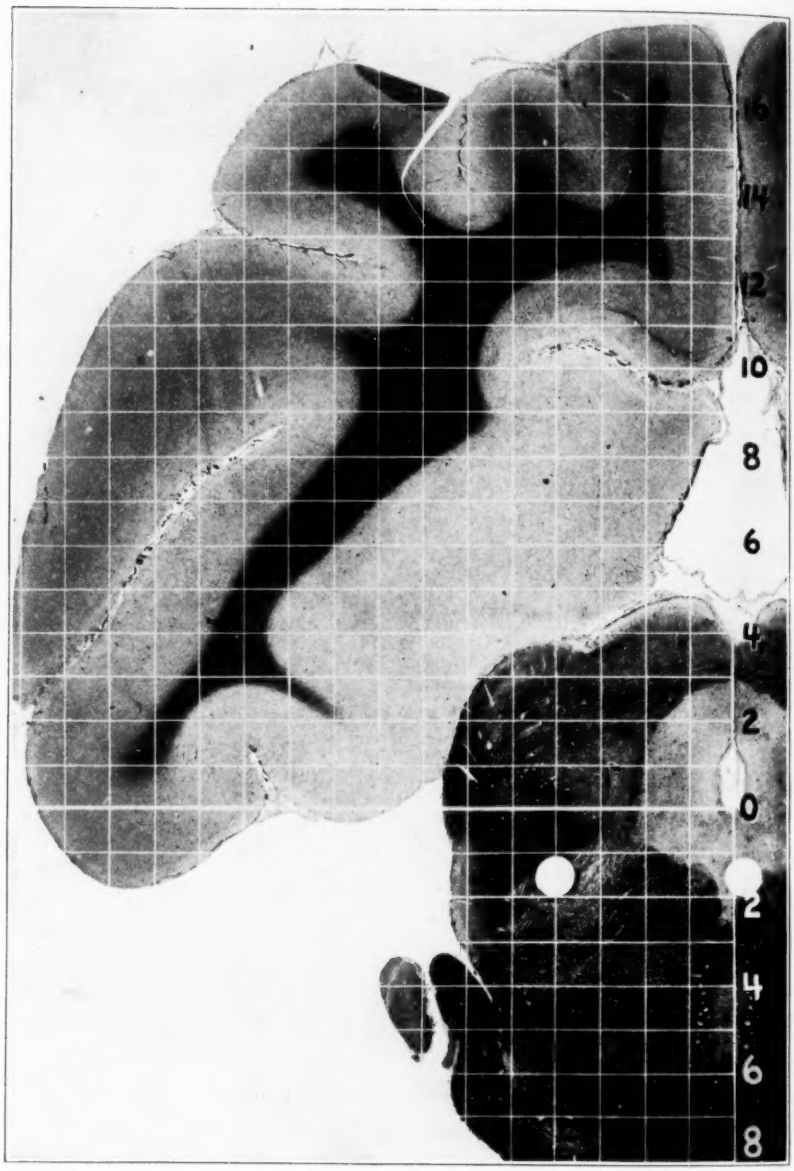

Fig. 14.—Photomicrograph of a section of the cat's brain in the frontal plane of the Horsley-Clarke instrument, 0.2 mm. in front of the interaural line.

TABLE 10.—*Data for Figure 14—Continued*

A	L	±			Optic Responses and Rhythms—Continued	
0	11.0	6.0			Loud, localized response, on effect	—
0	10.0	14.0 to 9.0			Response	—
0	10.0	13.0 to 9.0			Response	—
0	10.0	12.0 to 10.0			Response	Rhythm 4 a sec., stopped by light
0	10.0	6.0 to 5.0			Response	—
0	10.0	6.0 to 0.0	1.5	M	Huge response sharply on and off and continuous during light	No rhythm even in dark
0	10.0	6.0 to −2.0	0.0	M	Response	Rhythm appears after several on and off responses
0	8.0	18.0 to 12.0	16.0	M	Response	Rhythm 4 a sec., stopped by light
0	8.0	S to 12.0	14.0	M	Prolonged response at on and off; gone sharply at 12	Light in crossed eye gives volleys, which slowly change to true rhythm; when light off volleys reappear but fade into quiet background
0	8.0	18.0 to 7.0	14.0	M	Very strong, continued response and off effect and long after-discharge; large coarse response on jiggling light	Rhythm 4 a sec., stopped by light
0	8.0	12.0 to 3.0	3.5	M	Response	—
0	8.0	6.0			Good response	Rhythm appears in volleys when dark adapted
0	8.0	5.0			On and off responses	—
0	8.0	4.0			Good response; crossed greater than uncrossed	—
0	8.0	2.5			Loud, localized response little background	—
0	6.0	18.0 to 14.0	20	S	Response	Rhythm 3 a sec., stopped by light
0	6.0	12.0 to 7.0			Response	—
0	6.0	12.0			Crossed response	—
0	6.0	5.5			Response	Rhythm comes and goes
0	6.0	4.0			Good response; crossed greater than uncrossed	—
0	6.0	0.0 to −6.0	−1	M	Response	—
0	4.0	20.0 S to 14.0			Response	—
0	4.0	S to 12.0			Response	—
0	4.0	17.0 to 12.0			Response	—
0	4.0	15.0			Response	—
0	4.0	15.0 to 12.0			Good response, mainly crossed	—
0	4.0	4.0			Response	—
0	3.0	17.0 to 10.0			Response	Rhythm 1 a sec., stopped by light
0	3.0	3.0			Response with long after-discharge	—
0	2.0	22.0 S to 9.0	14.	M	Response	—
					Spontaneous Activities	
0	12.0	12.0 to 11.5			Crackling response, gone suddenly at 11.5	
0	8.0	16.0			Rhythm near heart rate but "beats" with it	
0	8.0	−7.0			Background	
0	6.0	11.0 to 8.0			Background	
0	6.0	5.5			Rhythm comes and goes	
0	6.0	3.0			Low frequency roar	
0	6.0	−2.5			Rhythm with respiration; spike discharges just preceding inspiration	
0	4.0	6.0 to −2.0	0	M	Background	
0	4.0	4.0 to 3.0			Background	
0	4.0	1.0			Background	
0	3.0	−2.0 to −3.0			Strong, sharply localized semirhythmic howls and some high-pitched discharges	
0	2.0	4.0 to −2.0			Background; heart rhythm	
0	2.0	−2.0 to −6.0	−4	M	Background	
0	2.0	−7.0			Crashes	
0	0.0	12.0 to −4.0	−3	M	Background waxes and wanes	

TABLE 11.—*Data for Figure 15*

A	L	±	Structures	
1.7	11.0	10.0	Posterior suprasylvian and lateral gyri	
1.7	10.0	2.0	Posterior splenial gyrus	
1.7	9.0	4.0	Posterior splenial sulcus	
1.7	8.0	—2.0	Cerebellum	
1.7	6.0	—2.0	Tectopontile tract	
1.7	6.0	—4.0	Brachium pontis	
1.7	5.5	—3.0	Lateral lemniscus	
1.7	5.0	3.0	Inferior colliculus	
1.7	3.0	—2.0	Dorsolateral tegmental region	
1.7	3.0	—4.0	Superior cervical brachium	
1.7	3.0	—7.0	Pons	
1.7	1.0	13.0	Splenial gyrus	
1.7	1.0	3.5	Commissure of inferior colliculi	
1.7	1.0	—3.0	Fourth nucleus	
1.7	0.5	0.0	Aqueduct of Sylvius	
1.7	0.5	—2.5	Posterior longitudinal bundle	
1.7	0.0	—5.0	Forel's decussation and Gudden's nucleus	
1.7	1.0	—6.0	Interpeduncular ganglion	
			Auditory Responses	
1.7	12.0	2	Response to tick	
1.7	10.0	2 to 0 M	Response to tick	
1.7	10.0	—2 to —3	Response to tick	
1.7	8.0	—2 to —4	Response to tick	
1.7	4.0	0	Response to tick	
			Somesthetic Responses	
1.7	8.0	0	Crossed paws; touch and bending; faint response	
1.7	8.0	0 to —2	Crossed paws	
1.7	4.0	—3	Crossed forepaw; strong touch response; loud background	
1.7	2.0	—2	Crossed forepaw; touch and bending	
1.7	2.0	—4	Crossed forepaw, feeble response	
1.7	2.0	—6	Crossed forepaw	
1.7	2.0	—7	Crossed forepaw; some from uncrossed	
			Optic Responses and Rhythms	
1.7	14.0	11 S to 7.0	Faint response	—
1.7	14.0	0 to —1.0	Faint response	—
1.7	12.0	14 to 9.0	On and off responses	Volleys at off, which fade to a quiet background and return on further illumination
1.7	12.0	S to 12.5	Faint response	—
1.7	12.0	14 to 8.0 9 M	Response	Rhythm 2.4 a sec. (heart 2.7 a sec.)
1.7	12.0	5 to 4.0	Huge on and off responses; long after-discharge	After-discharge fades into loud background; stopped by light
1.7	12.0	2 to —1.0	Continued response during 1 min.	—
1.7	10.0	15	On and off responses, with bursts	Rhythm
1.7	10.0	12	Faint response	—
1.7	10.0	8 to 5.0	Response	Loud, nonrhythmic background stopped by light
1.7	10.0	5	Huge response	Rhythm 2-3 a sec., semiregular
1.7	10.0	4 to 2.5	Uncrossed response; compound bursts at on and off; increased after dark adaptation	—
1.7	8.0	S to 17.0 M	Huge response; distinct on and off to finger movement	Volleys on turning off light fade to quiet background but return again on further illumination
1.7	8.0	S to 13.0	Faint response	—
1.7	8.0	13 to 5.0 7 M	Response at on has 4 separate bursts	—
1.7	8.0	8	Crossed response; 2 waves / for on	—
1.7	8.0	4 to 1.0	Response of different quality than at 8 (above)	Rhythm during illumination after dark adaptation
1.7	8.0	3 to —1.0 0 M	Very strong on and off responses; crossed greater than uncrossed	—
1.7	6.0	S to 8.0	Faint response	—
1.7	6.0	2 to 0.0	Faint response	—
1.7	4.0	S to 10.0	Response	—
1.7	4.0	2 to 0.0	Very strong response; short after-discharge	—
1.7	4.0	2	Response	—
1.7	2.0	16 S to 11.0	Crossed response	—
1.7	2.0	S to 12.0	Very strong response	—
1.7	2.0	9 to 6.0	Response	—
1.7	2.0	5 to 2.0	Very strong response	—
1.7	2.0	3	Response	—
1.7	2.0	3 to 2.0	Response	—
1.7	2.0	2 to 1.0	Strong high-pitched response	—
			Spontaneous Activities	
1.7	10.0	3.0	Sudden decrease in background	
1.7	10.0	—1.5	Sudden loss of background	
1.7	2.0	5.0	Rhythm of 15-20 a sec. suddenly appears	
1.7	2.0	2.0 to —9.0	Howl	
1.7	2.0	—0.5	Howl	

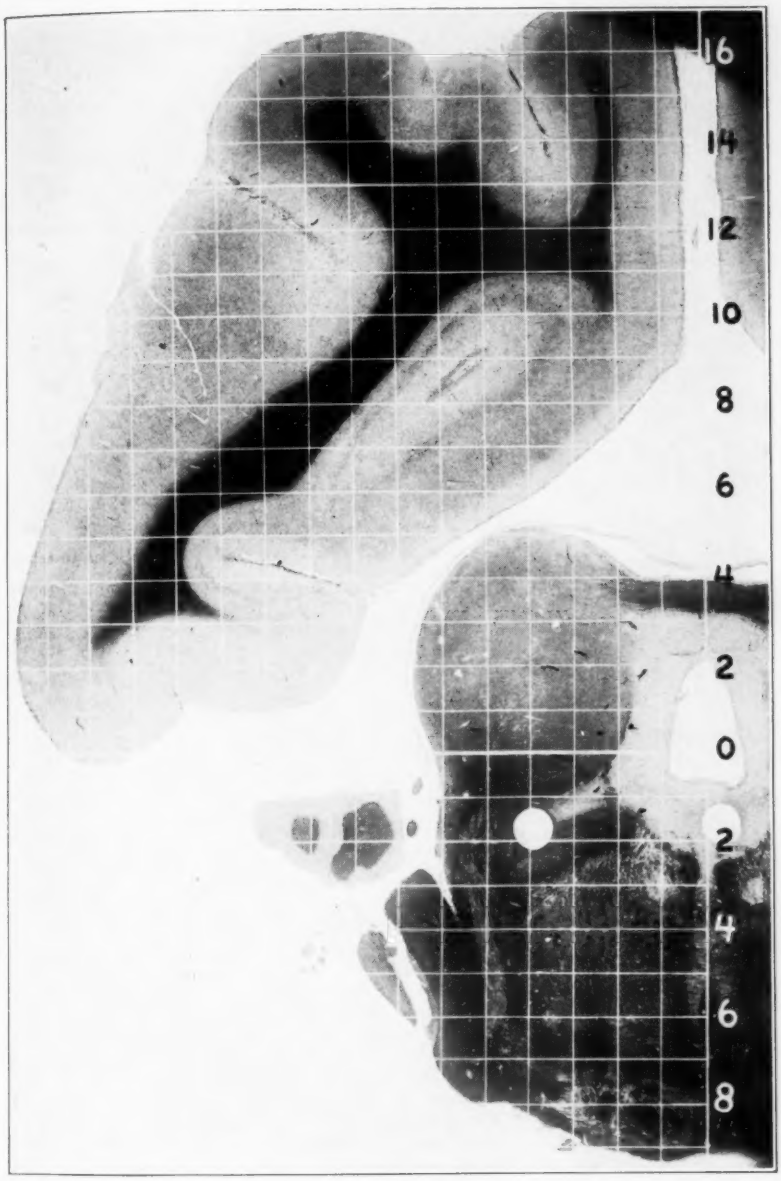

Fig. 15.—Photomicrograph of a section of the cat's brain in the frontal plane of the Horsley-Clarke instrument, 1.7 mm. behind the interaural line.

TABLE 12.—*Data for Figure 16*

A	L	±	Structures	
3.6	8.0	—5.0	Ventral acoustic nucleus	
3.6	8.0	—5.5	Vestibular nerve	
3.6	7.0	—5.5	Trapezoid body	
3.6	6.5	—5.0	Spinal fifth tract	
3.6	6.0	—3.0	Brachium pontis	
3.6	5.0	—2.0	Ventral spinocerebellar tract	
3.6	5.0	—6.0	Trapezoid body and root of facial nerve	
3.6	4.0	3.0	Inferior colliculus	
3.6	4.0	—2.0	Uncinate tract of Russel	
3.6	4.0	—7.0	Superior medial parolivary nucleus	
3.6	3.0	—2.0	Superior cerebellar brachium	
3.6	3.0	—3.0	Bechterew's nucleus	
3.6	3.0	—8.0	Trapezoid body	
3.6	2.5	—1.5	Mesencephalic root of fifth nerve	
3.6	2.0	—2.0	Central gray matter of floor of fourth ventricle	
3.6	2.0	—4.0	Reticular formation (Gudden's nucleus)	
3.6	2.0	—8.0	Trapezoid body	
3.6	1.0	—2.5	Nucleus proprius of central gray matter	
3.6	1.0	—5.5	Reticular formation (predorsal bundle and ventral nucleus)	
3.6	1.0	—9.0	Pyramidal tract	
3.6	0.5	—8.0	Medial lemniscus	
3.6	0.5	—3.0	Posterior longitudinal bundle	
3.6	0.0	4.0	Vermis	
			Auditory Responses	
4.0	8.0	6 to —6 —2 M	Change of character of response at —3	
3.0	6.0	1	Response to tick	
3.6	6.0	—1 to —4	Faint response to tick	
3.0	4.0	5 to 2	Response to tick	
3.0	4.0	2	Faint response to tick	
3.6	4.0	0 to —6	Response to tick	
3.0	4.0	0 to —2	Response to tick	
3.6	4.0	—1 to —4	Response to tick	
3.6	4.0	—5	Response to tick	
3.6	2.0	5 to 1 4 M	Response to tick	
3.6	2.0	4	Faint response to tick	
			Somesthetic Responses	
6.0	7.0	3 to 0	Legs (hindleg best) and body; not to touch but to tap or vibration	
6.0	7.0	0 to —3	Legs (foreleg best) and body; not to touch but to tap or vibration	
3.0	7.0	—3 to —5	Crossed legs and body	
3.0	6.0	—4	Crossed legs and body	
3.0	4.0	—5	Crossed legs and body	
3.6	4.0	—6	Forepaw; touch and bending; strong response	
3.6	2.0	—4	Body wall	
			Optic Responses and Rhythms	
4.0	12.0	17.0 S to 7 M	Crossed greater than uncrossed; low-pitched, coarse response	
8.0	12.0	14.0 S	Response	
6.0	7.0	14.0 to 10 M	Response	
3.0	7.0	8 to 10	Response	
3.0	7.0	8 to 9	Response	
6.0	7.0	7.0	Response	
3.6	6.0	8 to 10	Good response	
3.0	6.0	8 to 10	Response	
3.0	6.0	8 to 9	Response	
6.0	4.0	19.5 S to 14	Response	
3.6	4.0	8 to 11	Response	
3.0	4.0	8 to 10	Response	
3.0	4.0	17.0 S	Response	
3.0	4.0	16.0 to 4 10 M	Loud response	Rhythm 5 a sec., waxes and wanes
6.0	4.0	14.5	Low-pitched, coarse response	
6.0	4.0	9.0	High frequency, fine response	
3.6	4.0	4.0	Response	
3.6	2.0	8 to 11	Response	
3.0	2.0	8 to 11	Response	
3.6	2.0	18.5 to 11	Response	
3.6	2.0	6.0 to 4	Faint response	
3.6	2.0	6.0	Faint response	
3.6	0.0	1.0	Response	
			Spontaneous Activities	
3.0	4.0	1.0 to —1	Background	
3.6	4.0	0.0	Howl	
3.6	2.0	—1.0	Huge background; heart rhythm present	
3.0	2.0	—2.0 to —4	10 a sec. semirhythm	
3.0	2.0	—3.0	Huge roar	
3.6	2.0	—3.5	Rhythm synchronous with heart	
3.0	2.0	—5.0	Howl	
3.0	2.0	—7.0	Huge howl	
3.6	0.0	—2.5	Huge background; alternating periods of quiet and continuous or rhythmic discharges	
3.6	0.0	—5.0	Roar	

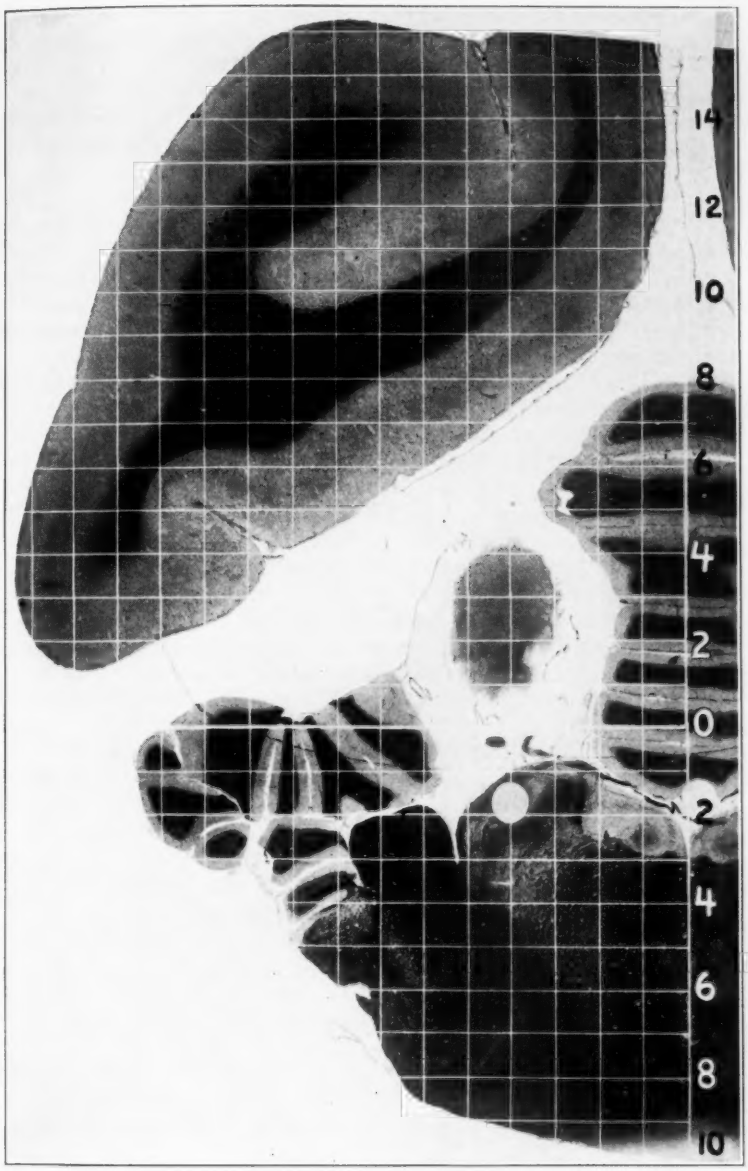

Fig. 16.—Photomicrograph of a section of the cat's brain in the frontal plane of the Horsley-Clarke instrument, 3.6 mm. behind the interaural line.

DISCUSSION

Dr. John F. Fulton, New Haven, Conn.: About thirty years ago, when the string galvanometer was first introduced, a great many studies were carried out, principally under the stimulus of Professor Piper, on the electromyogram: electromyograms of voluntary contraction, of postural contraction and of other forms of activity of skeletal muscle. Piper described a dominant rhythm of 40 or 50 per second which he believed to characterize the discharge of the neurons involved in voluntary contraction. It was later pointed out that certain forms of postural response did not have any recognizable electromyographic curve; the responses were extremely small. On the basis of this observation it was thought that postural responses were mediated by some mechanism quite different from that for voluntary responses. For about twenty years a controversy waged, which ultimately came to little, until Adrian and Denny-Brown and others succeeded in isolating the single unit. It was then found that the 50 per second rhythm of Piper meant absolutely nothing, that the rate of discharge from the central nervous system varied from 200 per second in voluntary responses to 5 to 10 per second in postural responses, that any highly organized response was carried out by units in complete temporal dispersion and that the algebraic summation of electrical effect which one saw in the electromyogram indicated little as to the fundamental character of the response of individual units.

Now this is a rather long preamble, and I apologize for it, but I think that the same principles apply to the newer studies of brain action potentials. The observed rhythms may or may not be significant: i. e., they may or may not indicate the fundamental rhythm of individual units within the brain. I wish to call attention to the point mentioned by Dr. Gerard which Professor Adrian emphasized last year before this association—that in sleep the occipital Berger rhythm is very pronounced but when activity occurs the Berger rhythm diminishes, sometimes almost completely. In other words, with asynchronism of unitary discharge among the myriad of units in the occipital lobes, the electrical effect is nil. It seems to me, in view of this fact, that one is likely to burn one's fingers, just as those persons did who studied electromyograms a number of years ago, if one attempts to infer from the observed rhythm the character of the activity of individual units. A square millimeter of brain surface has underlying it 20,000 neuron units, and the thought that a gross record of the electrical effect from a small area of this sort gives any knowledge of the discharge of any individual units in this extraordinary constellation is to me not plausible.

I should like to congratulate Dr. Gerard for being among the first to analyze the problem in rigorous physiologic terms. I do not think that any statement he made this morning can possibly be misinterpreted, and I welcome it as a step toward an adequate physiologic analysis of the problem.

I should like to ask him one question. In the first sentence of his abstract he said that nerve cells are capable of spontaneous discharge. By that I suppose he means that nerve cells can be caused to discharge without sensory innervation. I should like to ask him what evidence there is for this statement. It brings up a philosophic point, for some investigators feel that nerve cells never discharge unless an afferent impulse reaches them.

Dr. Lawrence Kubie, New York: I should like to ask Dr. Gerard one question along the lines of Dr. Fulton's question. Does any one have any idea of the fate of these discharges? Is it safe to assume that where there is an electrical impulse there is a nervous impulse, or is this going a step beyond the present knowledge? If this is true, then one has to think of these discharges as traveling along axons and coming into contact through synapses with other neurons, which

means that the picture of the nervous system becomes one of an almost chaotic array of discharging elements, discharging either with the chaotic lack of pattern of cosmic rays, or else of brownian movement traveling along certain partially organized circuits. Considerations of this kind once gave me the courage to describe hypothetic pathways of irregular closed circuits for such discharges in the nervous system. Without such a system of closed circuits, it would seem to me that one would have to assume some form of degradation of energy in the nervous system whereby these discharging impulses would be degraded into lower forms of energy without known neurologic sequelae.

DR. GASSER: One thing about Dr. Gerard's records that impressed me is the extreme lability of the waves which he has pictured in the central nervous system. This feature of the records claimed my attention because it raised the question of what might be the basis for this lability. I think of electrical potentials in terms of nerve fibers as samples of nerve tissue in general. Certain processes produce potentials in nerve fibers, and it is possible that analogous processes may occur in all parts of neurons.

The transmission of a message in a nerve is brought about by a process giving a potential, which is called the spike. This potential is almost constant in its properties, even beyond the possible range of physiologic conditions. It never changes its shape, although it may undergo a small variation in the size and velocity of transmission. In peripheral nerves there are, however, other processes which produce potentials called "after-potentials," and these are extremely labile in their manifestations. One may imagine that there are in the central nervous system potential-producing processes akin to those producing after-potentials in nerve fibers; in fact, there is evidence that such processes are present in the spinal cord and that the irritability of the cord behaves as one would expect on the basis of the potentials found.

Dr. Gerard has spoken of the rhythmicity of neurons. It is an interesting fact that one can obtain rhythmic activity in the after-potentials of isolated nerves. While such rhythms, as compared with those in neurons in position in the nervous system, may represent a corrupt form of rhythmicity, they have the merit of being accessible for study. Dr. Lehmann in my laboratory has shown, for example, that the waves are decreased in size by the addition of calcium and prolonged by an increase of carbon dioxide. Whether or not such waves may be placed in analogy with those Dr. Gerard has pictured in his slides, one cannot fail to attach some importance to the fact that they are affected in the same way by the same agents.

DR. R. W. GERARD, Chicago: I am grateful to Dr. Fulton for sounding, with more clarity than I had dared, a warning against too rapid a direct application of these new technics to clinical problems. There obviously will be a tremendous temptation to dash in and take electro-encephalograms in any and all conditions; without question, the pioneer work will have to be largely empirical in this field. It is well to have an authoritative warning of the many pitfalls on the way.

As to the questions of the localization of these potentials and the confusion due to the activity of many individual neurons, these are, of course, the problems that have been faced for years in working with the nervous system. I recall the classic remark of some Harvard workers that an attempt to analyze discharges in nerves containing many fibers is as hopeless as trying to deduce the properties of an egg from those of an omelet.

It is possible at present, however, to get down either to the single unit in the case of the peripheral nerve or to a very small group of closely related units, even in the central nervous system. In all this work, for example, we have used a concentric electrode, sacrificing sensitivity enormously for the sake of sharpness

of localization. The attempt to get activity in isolated portions of the nervous system has been pursued from that point of view. We have spent a good deal of time, with no success, in trying to get potentials from the isolated cerebrum of the embryonic chick. I am therefore particularly happy that we have now obtained these regular rhythms from the fully isolated cerebrum, and particularly the olfactory bulb, of the frog, in which it will be possible to examine in detail some factors controlling the synchronous beat of a mass of neurons.

I am not quite certain what additional evidence Dr. Fulton would ask to prove that nerve cells can beat spontaneously—spontaneously only in the sense, as he correctly stated, of continuing in the absence of specific afferent impulses. When a group of isolated nerve cells lie on cotton and nothing is done to them, they certainly do not receive regular stimuli, for instance, 5 a second. That there are continuous stimuli is, of course, the burden of my discussion today. There must be certain constant stimuli or, perhaps better, constant conditions which determine these rhythmic activities in nerve cells. These, however, will, I believe, prove to be primarily chemical rather than neural.

In regard to Dr. Kubie's searching question on the confusion of impulses chasing each other regularly over the entire nervous system, I do not believe that most of the large, regular electrical potentials that one observes in neural masses prove the passage of nerve impulses. I differ on this point with Adrian's second position and that of certain other workers in the field and am inclined to attribute especially the slow potentials largely to electrical variations within the cells themselves, which are not transmitted along axons and which modify the potential activity of a mass of nerve cells rather than indicate the discharge of impulses from them.

There is not time, of course, to develop the general picture of neural activity that is emerging, but may I compare the situation with that in the problem of the peripheral nerves a decade or two ago? The earlier pictures of the nerve impulse were of energy, substance or a mechanical wave of some kind thrown into a nerve fiber at one end and passively transmitted until it emerged at the other end. Recent work has exploded such a view, and it is known that the nerve fiber actively transmits the nerve impulse. In the same way, I think one has tended to consider the central nervous system as a passive aggregate of nerve cells waiting, more or less willingly, to be stimulated by nerve impulses and, between impulses, doing nothing. I cannot believe that this is nearly the correct picture of the central nervous system. It is rather in a state of continual activity, with fluid patterns developing and disappearing, and particular entering impulses only, so to speak, ripple the patterns already there, temporarily disturbing the balance in the cells, which then settle back into some dynamic pattern. Such a view in no sense tends to throw overboard any of the known localizations but is something additional to them.

Possibly these comments have also answered in part Dr. Gasser's very proper question as to how these potentials can be so fluid when the spike in peripheral nerve is such an extremely constant electrical phenomenon. If these potentials are not spikes, even if they represent but a statistical and irregular addition of various such states, one could not, of course, expect such constancy in the central nervous system.

The comments on carbon dioxide and after-potentials deserve more consideration than is possible at the moment.

PICK'S DISEASE

CLINICOPATHOLOGIC STUDY WITH REPORT OF TWO CASES

ARMANDO FERRARO, M.D.
AND
GEORGE A. JERVIS, M.D.
NEW YORK

The form of presenile psychosis known as Pick's disease was first described in 1892, by Arnold Pick,[1] of Prague, who recorded a series of cases [2] in which progressive dementia was invariably associated with aphasia occurring in old age and in which autopsy showed circumscribed atrophy of the cerebral cortex. Up to the present time about seventy pathologically verified cases have been reported, and both the clinical and the pathologic aspects of the disease have been the object of painstaking investigations.

The age of onset falls generally between 45 and 60 years, in the so-called presenium. Women are more affected than men, the ratio being 2:1. The duration of the disease is from two to ten years; the course is progressive and the prognosis decidedly ominous. Acute and chronic forms have been distinguished.

Clinically the disease is characterized by the association of progressive psychosis with neurologic signs of gradual onset. The mental picture belongs to the organic type commonly encountered in cases of senile dementia. In early stages, however, peculiar mental signs often occur which may be interpreted as due to lesion of the frontal lobes rather than to common intellectual deterioration. In fact, among the

---

From the Department of Neuropathology of the New York State Psychiatric Institute and Hospital.

1. Pick, A.: Ueber die Beziehungen der senilen Hirnatrophie zur Aphasia, Prag. med. Wchnschr. **17**:165, 1892.

2. Pick, A.: Die umschriebene Hirnatrophie als Gegenstand klinischer und anatomischer Forschung, in Arbeiten aus der deutschen psychiatrischen Universitäts-Klinik, Berlin, S. Karger, 1908, p. 20; Studien zur Lehre von Sprachverständnis, in Beiträge zur Pathologie und pathologischen Anatomie des Centralnervensystem, Berlin, S. Karger, 1898, p. 15; Senile Hirnatrophie als Grundlage von Herderscheinungen, Wien. klin. Wchnschr. **14**:403, 1901; Ueber Symptomcomplex bedingt durch die Combination subkorticaler Herdaffectionen mit seniler Hirnatrophie, ibid. **14**:1121, 1901; Ueber eigentümliche Sehstörungen in senilen Dementen, Jahrb. f. Psychiat. u. Neurol. **22**:35, 1902; Zur Symptomatologie der linkseitigen Schläfenlappenatrophie, Monatschr. f. Psychiat. u. Neurol. **16**:378, 1904; Ueber einer Symptomcomplex der Dementia senilis bedingt durch umschriebenen Hirnatrophie, ibid. **19**:97, 1907.

signs most frequently observed are: fluctuation of attention, akinesis, lack of initiative, defect of memory in the form of difficulty in the reproduction and acquisition of engrams, inability to acquire new material or to appreciate new situations as a whole, affective changes, tendency to jocularity and impairment of ethical and social behavior. Hallucinations, delusions, retrospective falsifications and confabulations are exceptional. With progress of the disease the mental picture becomes less characteristic and cannot be differentiated from that of other forms of profound organic dementia.

The neurologic symptoms are essentially the expression of focal lesions of the cerebral cortex: aphasia, agnosia, apraxia, alexia, agraphia, astereognosis and cortical blindness. Among these, aphasia of all varieties is the most frequent and may dominate the clinical picture from the beginning. In almost all cases, moreover, there is progressive deterioration of the speech faculty, which is finally reduced to a few stereotyped and often echolalic phrases. Epileptiform seizures are rare and generally occur only in the later stages, but peculiar attacks of general muscular hypotonia have been reported by several authors. Extrapyramidal symptoms are common, whereas lesions of the pyramidal tract are rare and tardy in appearance.

The pathologic picture of the disease is characterized by atrophic changes in the cortex circumscribed to one or more lobes or parts of a lobe, the most frequent localizations being in the frontal and temporal regions.

Microscopically, the condition appears to be a degenerative process of neural atrophy with compensatory neuroglial hypertrophy. In addition, histopathologic peculiarities are generally present and consist of a curious swelling of nerve cells and of characteristic cytoplasmic inclusions, the so-called argentophilic bodies. Both lesions are considered to be quasipathognomonic of Pick's disease. Senile plaques, Alzheimer's neurofibrillary changes and arteriosclerotic lesions are generally absent.

While the main clinical and pathologic aspects of Pick's disease are well established, the problem of its nature is still unsolved and is the subject of much discussion. From the beginning of the history of the disease two divergent points of view were expressed: Pick,[1] without discussion, took for granted the senile character of the disease, whereas Reich [3] tried to establish its independence of senile processes.

---

3. Reich, F.: Ein Fall von alogischer Aphasie und Asymbolie, Allg. Ztschr. f. Psychiat. **62**:825, 1905; Der Gehirnbefund in dem vorgestellten Falle von Alogie, ibid. **64**:380, 1906; Aphasie oder Alogie, Arch. f. Psychiat. **46**:1234, 1910; Zur Pathogenese der circumscripten resp. systemartigen Hirnatrophie, Ztschr. f. d. ges. Neurol. u. Psychiat. **108**:803, 1927.

Subsequent speculations enlarged Reich's conception, stressing the analogy of Pick's disease to various well known heredodegenerative conditions. Thus, Richter [4] attempted a comparison between Pick's disease and familial amaurotic idiocy based on similar histopathologic changes of the nerve cells. Kufs,[5] Stief [6] and Kihn [7] compared Pick's disease to Huntington's chorea, claiming that the basic process, of endogenous and degenerative character, is essentially the same in the two conditions, the lesions in the former disease being predominantly in the frontal lobe and in the latter in the basal ganglia. Similar parallelisms were expressed by Spatz,[8] in an attempt to compare Pick's atrophy and Marie's cerebellar atrophy, and by Giljarowsky [9] who in his report of cases of Pick's disease pointed out the analogy to olivopontocerebellar atrophy. These views emphasizing the systemic electivity of the atrophic process uphold the theory expressed by Gans [10] that Pick's disease should be classified with the forms of heredodegenerative abiotrophy. New evidence has recently been added by Grünthal [11] and Braunmühl and Leonhard,[12] who reported the familial occurrence of the disease, and by Guillain, Bertrand and Mollaret,[13] who described a typical case in a man of 29.

In the United States little can be found in the literature concerning Pick's atrophy. Two clinical presentations (Hoedemacher and Matthews, and Nichols and Weigner [14]) and a preliminary report (Kahn and

4. Richter, H.: Eine besondere Art von Stirnhirnschwund mit Verblödung, Ztschr. f. d. ges. Neurol. u. Psychiat. **38**:127, 1918.

5. Kufs, H.: Beitrag zur Histopathologie der Pickschen umschriebenen Grosshirnrindenatrophie, Ztschr. f. d. ges. Neurol. u. Psychiat. **108**:786, 1927.

6. Stief, A.: Zur Kasuistik der Pickschen Krankheit, Ztschr. f. d. ges. Neurol. u. Psychiat. **128**:544, 1930.

7. Kihn, B.: Probleme der Choreaforschung, Nervenarzt **6**:505, 1933.

8. Spatz, H.: Anatomische Befunde eines Falles von präseniler Verblödung, Zentralbl. f. d. ges. Neurol. u. Psychiat. **40**:73, 1925.

9. Giljarowsky, W.: Zur Pathologie der Rückentwicklungsprozesse, Ztschr. f. d. ges. Neurol. u. Psychiat. **139**:509, 1932.

10. Gans, A.: Betrachtungen über Art und Ausbreitung des krankhaften Prozesses in einem Fall von Pickscher Atrophie des Stirnhirns, Ztschr. f. d. ges. Neurol. u. Psychiat. **80**:10, 1922.

11. Grünthal, E.: Ueber ein Brüderpaar mit Pickscher Krankheit, Ztschr. f. d. ges. Neurol. u. Psychiat. **129**:350, 1930.

12. von Braunmühl, A., and Leonhard, K.: Ueber ein Schwesternpaar mit Pickscher Krankeit, Ztschr. f. d. ges. Neurol. u. Psychiat. **150**:209, 1934.

13. Guillain, G.; Bertrand, I., and Mollaret, P.: Considérations anatomocliniques sur un cas de maladie de Pick, Ann. de méd. **36**:249, 1934.

14. (*a*) Hoedemacher, D., and Matthews, R.: Pick's Disease: A Preliminary Report, Arch. Neurol. & Psychiat. **28**:1449 (Dec.) 1932. (*b*) Nichols, I., and Weigner, W.: Pick's Disease: Review of the Literature and Presentation of Case, Arch. Neurol. & Psychiat. **32**:241 (July) 1934.

Thompson [15]) are in fact the only American contributions to the study of the disease.

In the present paper two cases will be described in their clinical and pathologic aspects, and the debated problem of the nature of the disease will be particularly discussed.

REPORT OF CASES

CASE 1.—*History and Clinical Findings.*[16]—W. L., a white man aged 58, a bookkeeper, was admitted to the Rochester State Hospital on Aug. 7, 1930. The family history failed to show any nervous or mental impairment in ancestors or collateral lines of two generations. The patient had always been healthy, and no diseases were recorded in his personal history. He was married to a healthy woman and had two children; one died at the age of 10, of appendicitis; the other was living and in good health. The patient attended a business institute and worked for various employers, always holding good positions. He was a cultured man and was fond of reading; he was always friendly and correct in his attitude toward others, sociable and fond of home and moderate in his habits.

In 1923, following a mild attack of influenza, the patient began to show a slow and gradual decline in interest and in business capacity. Whereas formerly he had been eager to help his wife, he then sat on the porch and watched her chop wood and do all sorts of hard work without the slightest effort to help her, not even making any comment. He also squandered a great deal of money in poor business deals without being concerned or worried about his failures. Two years later definite changes in his character became established; he grew irritable, rude to his family and friends, vulgar in his manner and careless regarding his personal appearance. About the same time he showed forgetfulness of names and of the location of places he wanted to visit; he occasionally failed to recognize close friends. Sometimes he met his daughter on the street without showing a sign of recognition. This, however, seemed due more to affective indifference than to lack of identification, for he was uninterested in his family's welfare and never inquired after his wife's or his daughter's business or health. For two or three years prior to his admission to the hospital he seldom did any reading, which formerly had been his favorite pastime. He was also suspicious and spoke at times about being watched and followed, though he did not seem to have hallucinations. For several months, two years before his admission, he had been excessively talkative and restless, his conversation being childish and about things of little interest. After this period of excessive talking, another period followed during which he seldom talked spontaneously and was generally brief and irritable in his replies to questions. Defect in speech, however, was never observed. The day before his admission the patient was caught turning in a fire alarm; as a result of his queer behavior he was committed to the state hospital for observation.

Physical Examination.—The patient was well nourished and appeared approximately 60 years of age. No signs of organic disease, particularly arteriosclerosis, were observed. The usual neurologic examination also gave normal results. Urinalysis showed nothing abnormal and the Wassermann reactions of the blood

15. Kahn, E., and Thompson, L.: Concerning Pick's Disease, Am. J. Psychiat. **13**:937, 1934.

16. The clinical record was furnished by Dr. J. L. Van De Mark, Superintendent of the Rochester State Hospital, Rochester, N. Y.

and the spinal fluid were negative. Further examination of the spinal fluid did not show any alteration.

Mental Status.—The patient was clean in habits and tidy in appearance. He helped little with ward work but for the most part sat apart, apathetic and indifferent to his surroundings and with a dull expression on his face. He seemed to be somewhat confused and at times wandered aimlessly about the ward. He cooperated passively in what was done for him and answered questions readily but briefly; he was never spontaneous in conversation and spoke in a low tone, without expression. During the interviews he was distractible, and his attention was difficult to hold; some questions he did not seem to appreciate.

No particular incoherence or irrelevance was observed in the stream of mental activity.

Emotional reaction was limited. Both his facial expression and his answers to questions showed deep indifference and apathy—a real affective emptiness.

No abnormal mental trends were observed. The patient denied having delusions. He seemed to have had some hallucinatory experiences, but they were not definite, and when he was questioned his replies were vague.

Orientation was fair; he knew where he was, where the hospital was located and the month and year, but not the day; he did not know what the hospital was. Remote memory was good; he answered correctly questions about his birth, school, marriage, children, occupation, etc. Recent memory did not seem as good as remote; for instance, he was not definite about the details of his admission. At times he refused to answer questions, saying "I can't think now." Retention and immediate recall showed impairment. He could not remember names of streets and addresses for five minutes, but he repeated eight digits correctly. Marie's three paper test and the word pair test were performed with some difficulty. Counting and simple calculations were executed fairly well. Reading was not tested because of poor eyesight. Writing was slightly tremulous and slow, but without abnormality. Insight was absent.

Tests for thinking capacity and attention confirmed the difficulty in thinking, the instability of attention and particularly the inability to concentrate, which were the outstanding findings of the mental examination.

Course.—Developments in the hospital were characterized by slowly progressive mental deterioration. A few months after his admission the patient was always apathetic and uninterested. He did a little simple work about the ward, but he had to be watched and guided or he stopped work and wandered off without explanation. He did not retain things told him about his work. He answered a few introductory questions well but after a few words asked to be excused and walked out of the room. His answers were always exceedingly dull, and it was not possible to arouse his interest sufficiently to secure any intelligent discussion. There was pronounced lack of concentration. When he spoke there was some agitation in his hands, which were constantly picking. No neurologic signs and particularly no aphasic symptoms were elicited.

Examination six months later showed the same lack of interest and pronounced emotional loss; the inability to concentrate was also persistent. The patient did not give attention to questions, fussed with things on the table, hummed, looked around, drummed with his fingers, reached for things in his pocket and answered a few questions in a totally indifferent manner. He was only partially oriented.

One year later, the physical condition remained good, and neurologic examination continued to give normal results. Dulness, indifference and apathy had

increased. There was complete impairment of the whole intellectual activity. Disoriented and confused, he paid no attention to questions and seemed totally out of contact with his surroundings.

For the last two years of life the patient did not show any important new symptoms. This period was characterized by slowly progressive dementia and gradual diminution of spoken language, which was reduced to a few words and short sentences without any significance, repeated over and over. The state of advanced dementia prevented complete examination to detect whether the reduction of language was due partly to motor aphasia.

At the end of 1932 profound dementia had become established. The physical condition also gradually deteriorated. The patient lost weight and showed unsteadiness of gait; his general condition necessitated confinement to bed. In March 1933, two years and seven months after admission and about ten years after the probable onset of the disease, the patient died, with symptoms of pneumonia.

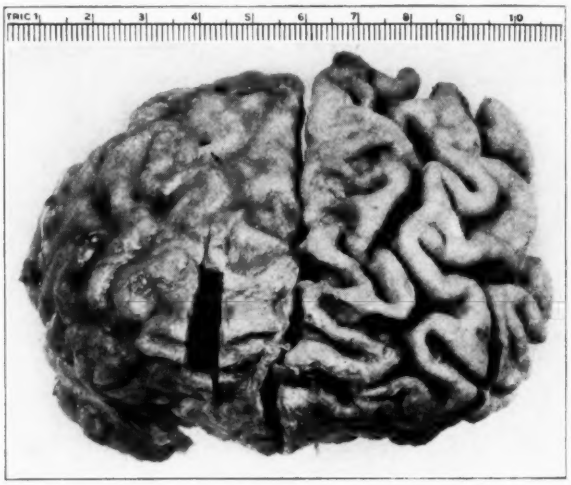

Fig. 1.—Photograph showing atrophy of the frontal lobe. On the right side the pia has been stripped from the cortex.

Gross Pathologic Observations.—Postmortem examination was performed twenty hours after death. The heart was normal; however, slight arteriosclerotic changes of the vessels were demonstrable microscopically. Two small atheromatous patches were observed in the aorta. The lungs showed bilateral foci of bronchopneumonia and a small abscess in the left lower lobe. The liver was congested, with fatty degeneration. The spleen had a septic appearance. Otherwise routine examination of the organs revealed nothing abnormal.

The brain weighed 1,230 Gm., the length on the basal aspect being 17 cm. and the greatest width 14 cm. The dura was rather firmly adherent to the skull but otherwise appeared normal. The pia was edematous, thick and slightly adherent to the convolutions, especially on the atrophic areas. The vessels of the base did not show arteriosclerotic changes. The lateral ventricles were considerably dilated.

The striking gross feature was marked shrinkage of the convolutions of the frontal and temporal lobes. The frontal atrophy involved the prefrontal lobe, being more pronounced in its anterior portion (fig. 1), and was symmetrical.

In the temporal lobe the atrophic process was more pronounced on the right side (figs. 2 and 3) and involved the second and third temporal gyri, whereas the first convolution and the hippocampus participated to a less degree. The parietal and the occipital lobe showed slight diffuse atrophy, with the exception of the cen-

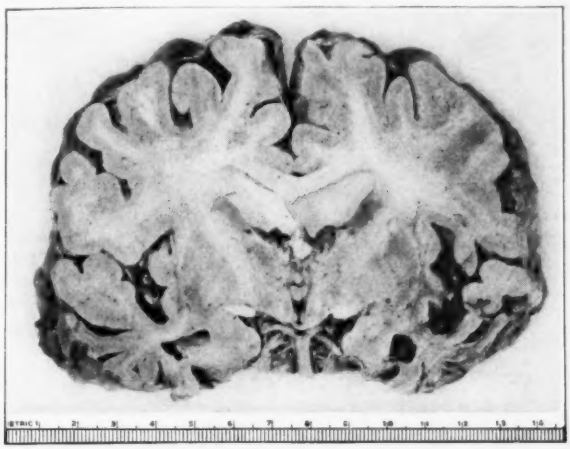

Fig. 2.—Photograph of a cross-section at the level of the anterior third of the corpus striatum, showing more pronounced atrophy of the right temporal lobe.

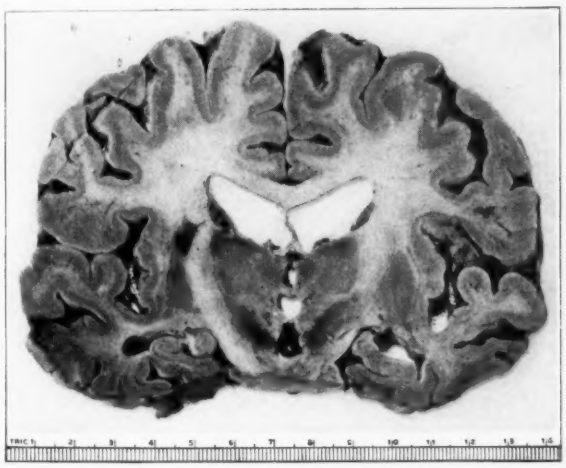

Fig. 3.—Photograph of a cross-section at the level of the anterior third of the thalamus, showing atrophy of the temporal lobe.

tral convolutions, which were of normal appearance. The cerebellum, pons and medulla oblongata also were slightly reduced in volume.

Microscopic Examination.—Sections of various areas of the brain were examined histologically with the following methods: Nissl's and Bielschowsky's for

nerve cells, Spielmeyer's and Weigert's for myelin sheaths, Holzer's and Ramón y Cajal's for glia, del Rio Hortega's for oligodendroglia and microglia, scarlet red and sudan III for fat products, Perdrau's for connective tissue, Turnbull's for iron and Weigert's for elastic fibers.

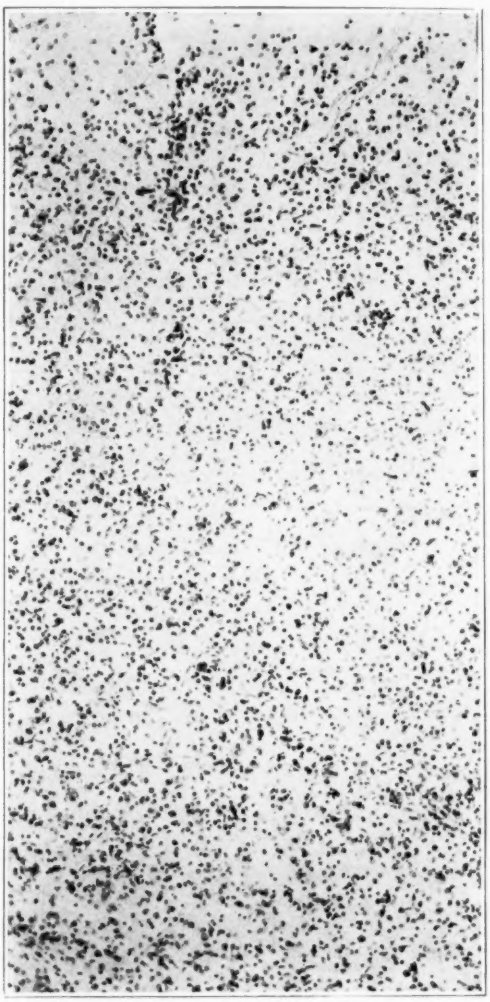

Fig. 4.—Photomicrograph of a section of the second frontal convolution, illustrating occurrence of cellular atrophy in all layers of the cortex. The few remaining cells are considerably altered, while glial nuclei are apparent in most of the tissue. Nissl's stain.

Meninges: A slight thickening resulting from an increase in fibrous tissue rather than from proliferation of cellular elements was observed over the areas of major atrophy.

Nerve Cells: With low power sections of atrophic convolutions stained with Nissl's method showed considerable diminution in the number of nerve cells, resulting in a deeply disturbed lamination. Areas were observed in which atrophy involved all layers of the cortex, a few shrunken nerve cells being scattered among proliferated glia cells (fig. 4). Figure 5 *A* illustrates another aspect of the cellular destruction involving all the cortical layers. In this section the glial reaction was very scanty in the middle and inner layers, while rich proliferation

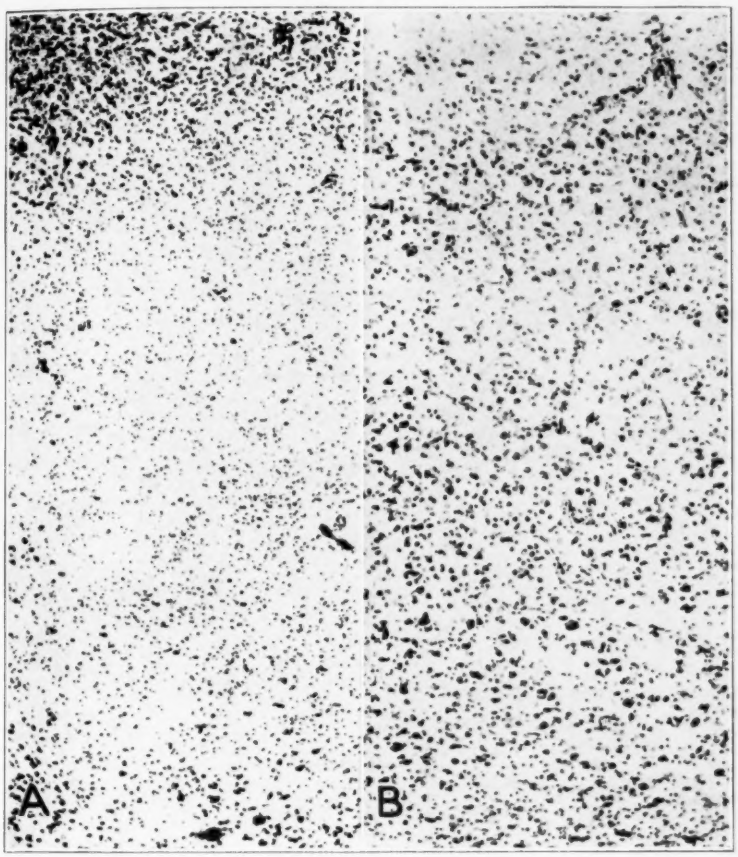

Fig. 5.—Photomicrographs (Nissl's stain) (*A*) of the third temporal convolution, illustrating destruction of the nerve cells in all cortical layers, with scanty glial reaction in the middle and inner layers and intense glial reaction in the external layer, and (*B*) of the first temporal convolution, illustrating the predominance of destruction of nerve cells in the third layer.

was seen in the external layer. In other zones destruction of nerve cells was more pronounced in the external layer, particularly the third (fig. 5 *B*). Occasionally areas were observed in which the atrophy seemed most extensive in the inner layers. Because of an identical proliferation of glia nuclei in the deep cortical layers and in the subcortical white substance, the boundary between the white and the gray

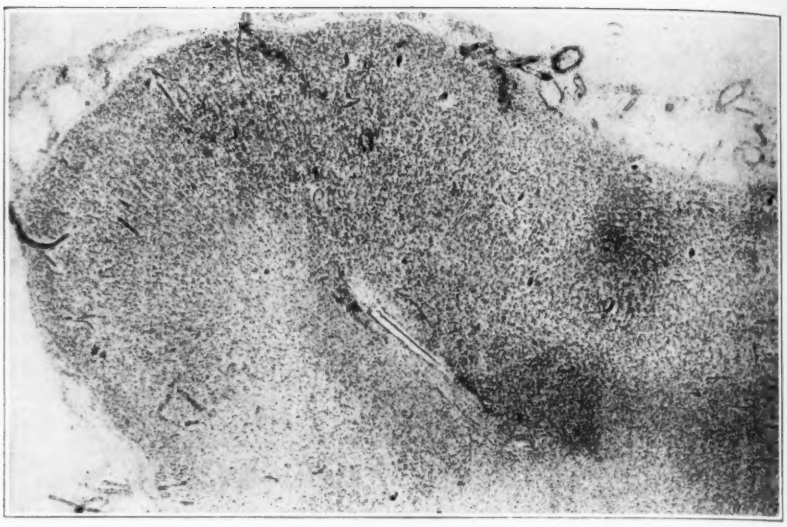

Fig. 6.—Photomicrograph of a section of the orbital convolution, illustrating the occurrence of abrupt demarcation between areas of various degrees of involvement. Nissl's stain.

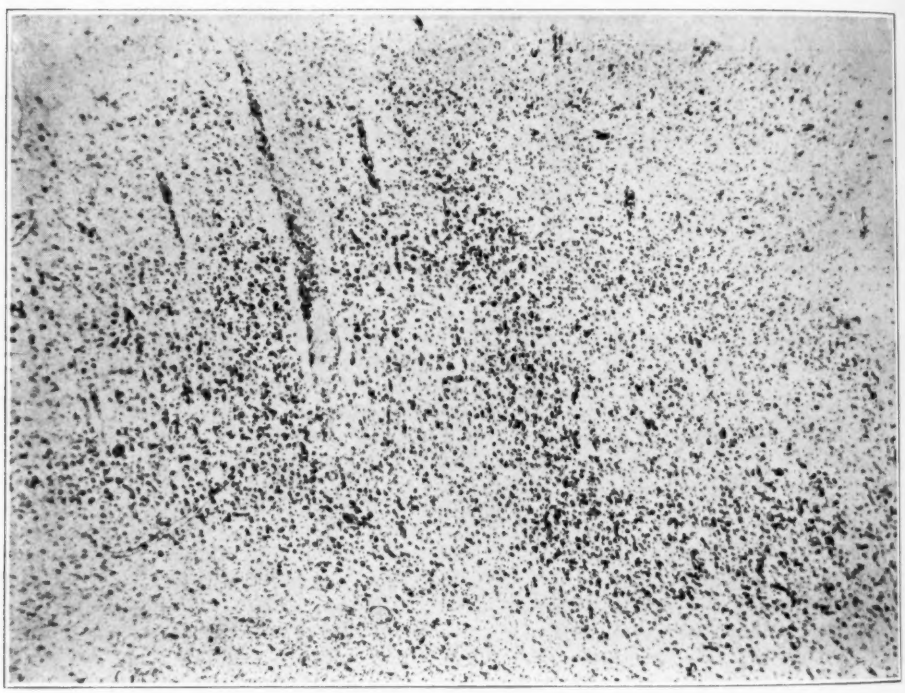

Fig. 7.—Photomicrograph of a section of the frontal lobe, showing abrupt demarcation between areas of involvement. On the left side of the large blood vessel the nerve cells are better preserved than those on the right. Nissl's stain.

matter disappeared in numerous areas. At times the process of atrophy resulted in status spongiosus, which occasionally produced tearing of the cortex in the middle layers.

The boundary between a better preserved area and an area of major involvement was often sharply demarcated, and zones were seen in which an almost abrupt passage occurred between an area of marked atrophy and one of almost normal tissue. Figure 6 illustrates the occurrence of such an abrupt demarcation

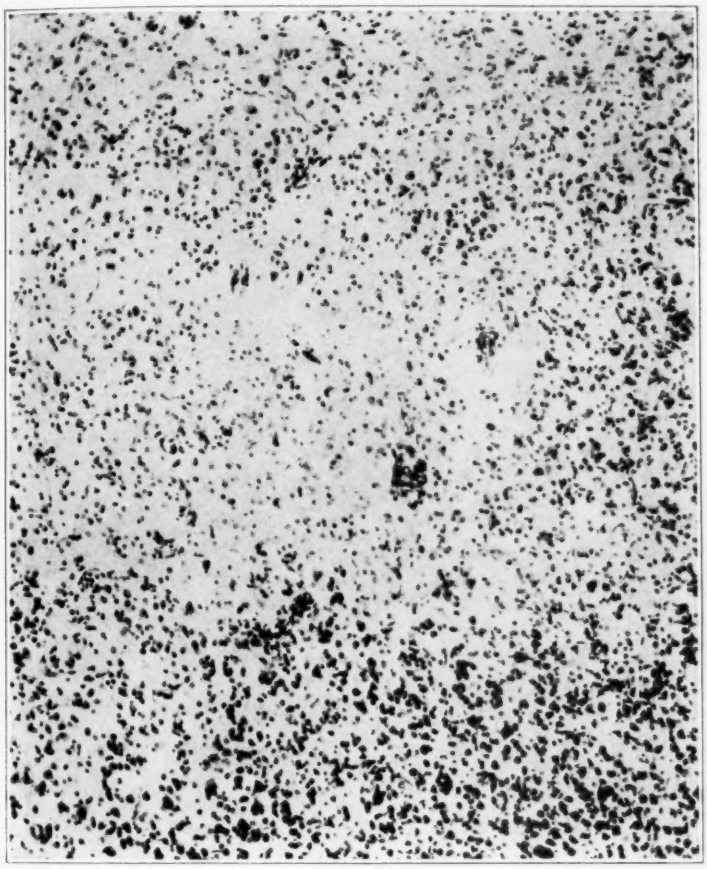

Fig. 8.—Photomicrograph of a section of the temporal lobe, illustrating the occurrence of a large patch in which the nerve cells surrounding the centrally located blood vessels have disappeared. Nissl's stain.

between variously involved areas on the two sides of the picture. In the central area the process of atrophy is accompanied by considerable proliferation of glial nuclei, whereas on the right and the left side the atrophy is less pronounced. The same abrupt demarcation between areas of various degrees of involvement is again illustrated in figure 7, in which much better preservation of cellular elements is seen on the left side of the largest blood vessel than on the right.

Moreover, patchy areas of destruction of nerve cells comparable to the acellular areas described in association with cerebral arteriosclerosis were frequently scattered in the cortex. At times such acellular areas surrounded one or more blood vessels and apparently involved the territory of their distributions. Figure 8 illustrates the occurrence of an irregular area in which the nerve cells have disappeared, particularly in the territory of distribution of the centrally located blood vessels.

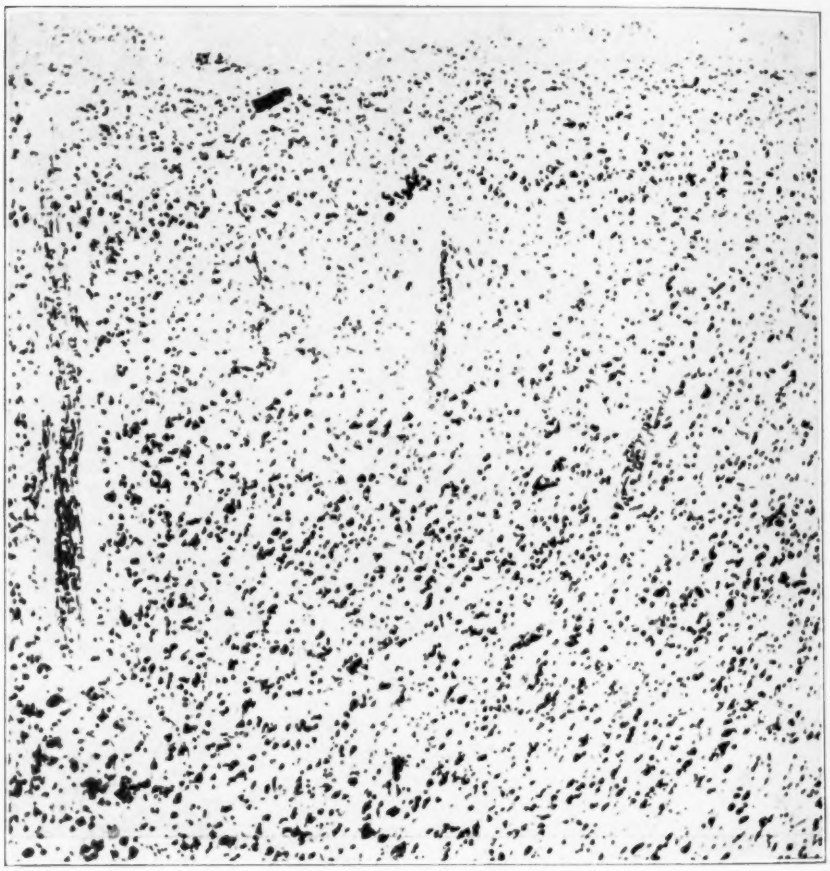

Fig. 9.—Photomicrograph of a section of the parietal lobe, illustrating areas of cellular rarefaction surrounding cortical blood vessels. Nissl's stain.

Surrounding the area, numerous nerve cells are seen intermingled with proliferated glial nuclei. In figure 9 also it may be seen that the centrally located blood vessel, which in this instance invaded the third layer, is surrounded by an area of considerable cellular rarefaction, which contrasts with a better preserved third layer in the remaining portion of the picture. In other instances there was proliferation of glia, of perivascular character (fig. 10).

The type of changes seen histologically in the nerve cells varied according to the intensity of the process. In the slightly involved areas nerve cells were reduced in volume, with either a concomitant loss of Nissl substance or hyperchromatosis of both the nucleus and the cytoplasm. In the severely involved areas this process of shrinkage was much more extensive. A few cells disclosed the so-called

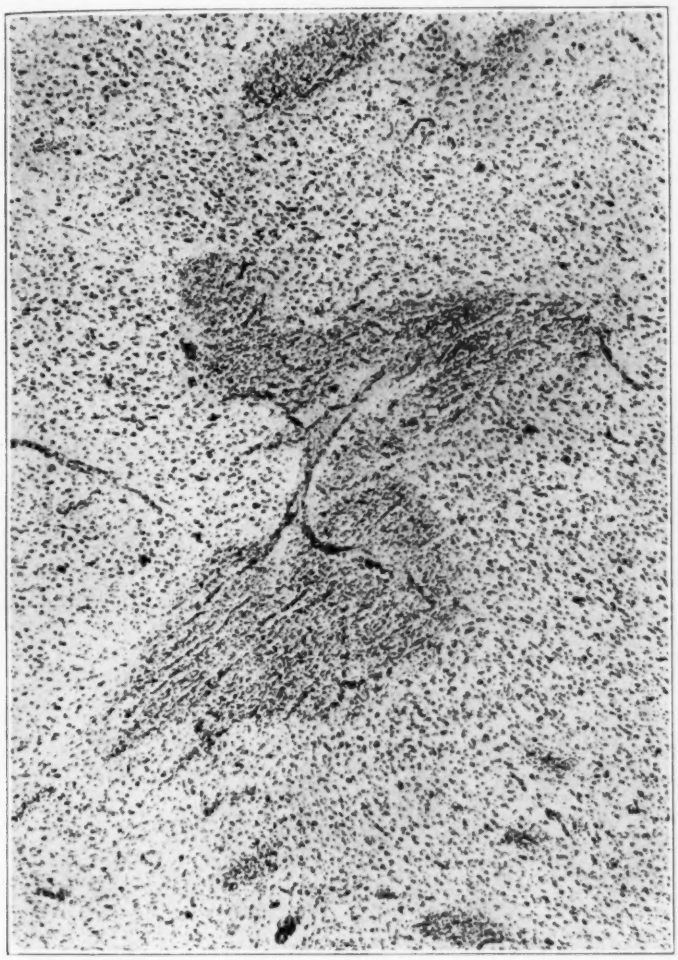

Fig. 10.—Photomicrograph of a section of the subcortical white matter of the temporal lobe, illustrating the occurrence of typical glial reaction surrounding the various branches of the centrally located blood vessel. Nissl's stain.

ischemic type of reaction. In better preserved cells, stains for fat showed an increased amount, which at times completely filled the cytoplasm.

Cellular changes of two types were seen which have been considered as typical of Pick's disease. One consisted of cellular swelling. The cytoplasm of the nerve cell, having lost most of its Nissl substance, appeared poorly stained except for a

thin perinuclear band. The nucleus either was normal or disclosed deformity and loss of chromatic substance (figs. 11 and 12). With Herxheimer's method fat substances were not detected in the swollen cells. The distribution of this lesion varied: It was practically absent in the areas of considerable atrophy and in the normal areas, whereas in slightly atrophic zones it was frequent. The second characteristic histopathologic lesion consisted of intracellular inclusions of argentophilic bodies, which were particularly numerous in the nerve cells of the cornu ammonis and were rare in other regions (fig. 13). They appeared as round homogeneous inclusions, the size of a nucleus. Occasionally degenerative structures which morphologically looked like argentophilic bodies were scattered free in the nerve tissue. However, it was difficult to identify them as such, par-

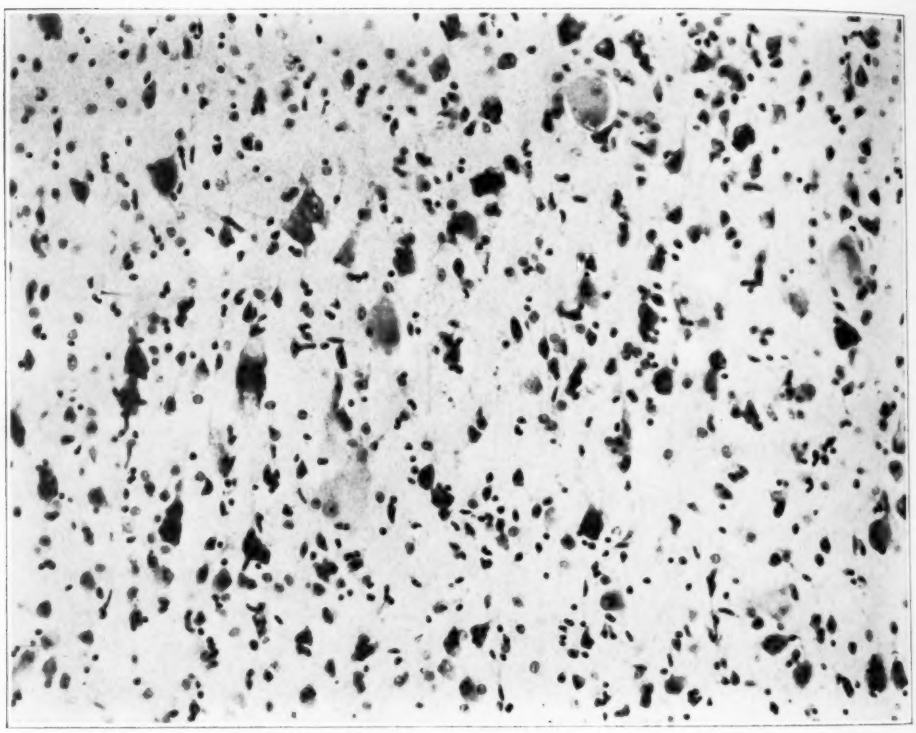

Fig. 11.—Photomicrograph of nerve cells in the first temporal convolution undergoing characteristic swelling. Nissl's stain.

ticularly when other products of disintegration disclosed an argentophilic character. Bielschowsky's method for neurofibrils failed to show senile plaques or Alzheimer's neurofibrillary changes.

The Weigert and the Spielmeyer stain for myelin disclosed destruction of the myelin sheaths, which was particularly severe in the most atrophic areas, that is, in the frontal and temporal lobes (fig. 14). In slightly involved areas swellings of the sheaths, giving the appearance of a rosary bead were often encountered, whereas in more severely involved areas the myelin sheaths were represented by remnants detectable as very small irregular fragments. The nerve fibers also had undergone a process of degeneration, consisting of gradual thinning of the axis-

cylinders and gradual disappearance of the fibers. There was little real fragmentation of the axons.

As already mentioned, the glial reaction was generally pronounced in atrophic convolutions. The gliosis was not, however, a necessary manifestation accom-

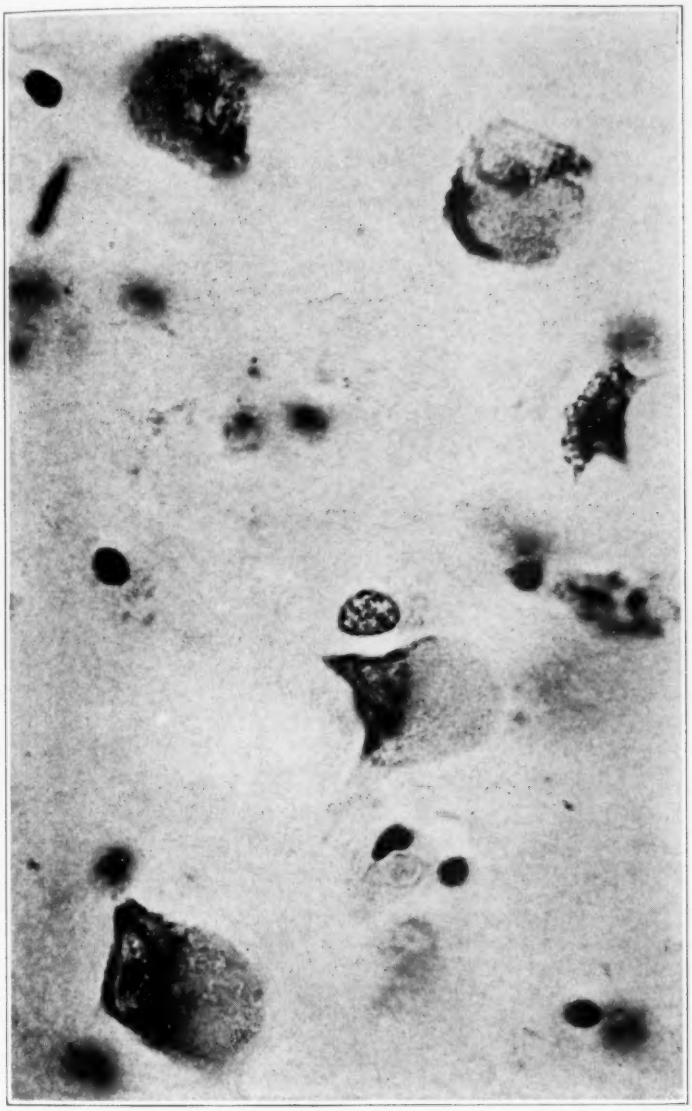

Fig. 12.—High power magnification of a portion of the caudate nucleus, showing cellular swelling. Nissl's stain.

panying the process of atrophy. In some areas the process of gliosis replaced the destroyed nerve cells in all cortical layers. In further areas, on the other hand, the gliosis was limited to a certain layer only, though destruction of the nerve

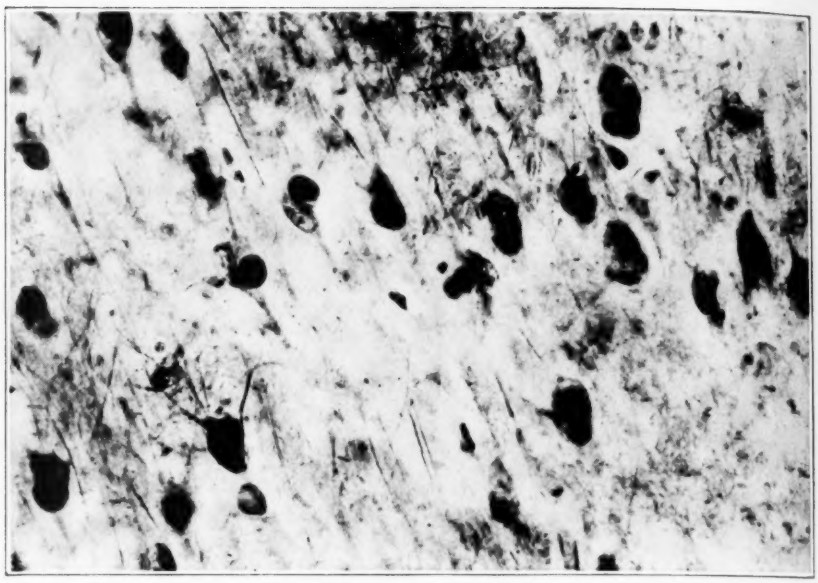

Fig. 13.—Photomicrograph illustrating the characteristic argentophilic bodies in the cells of Sommer's sector of the cornu ammonis. Cajal's silver stain.

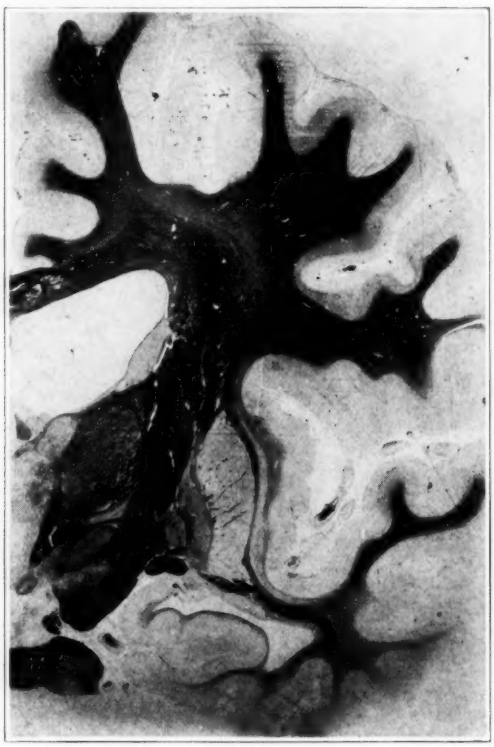

Fig. 14.—Photomicrograph illustrating demyelinization in the temporal lobe. Most of the myelin fibers in the lower portion of the field have disappeared, except for some of the fibers of the optic radiation. Weigert's stain.

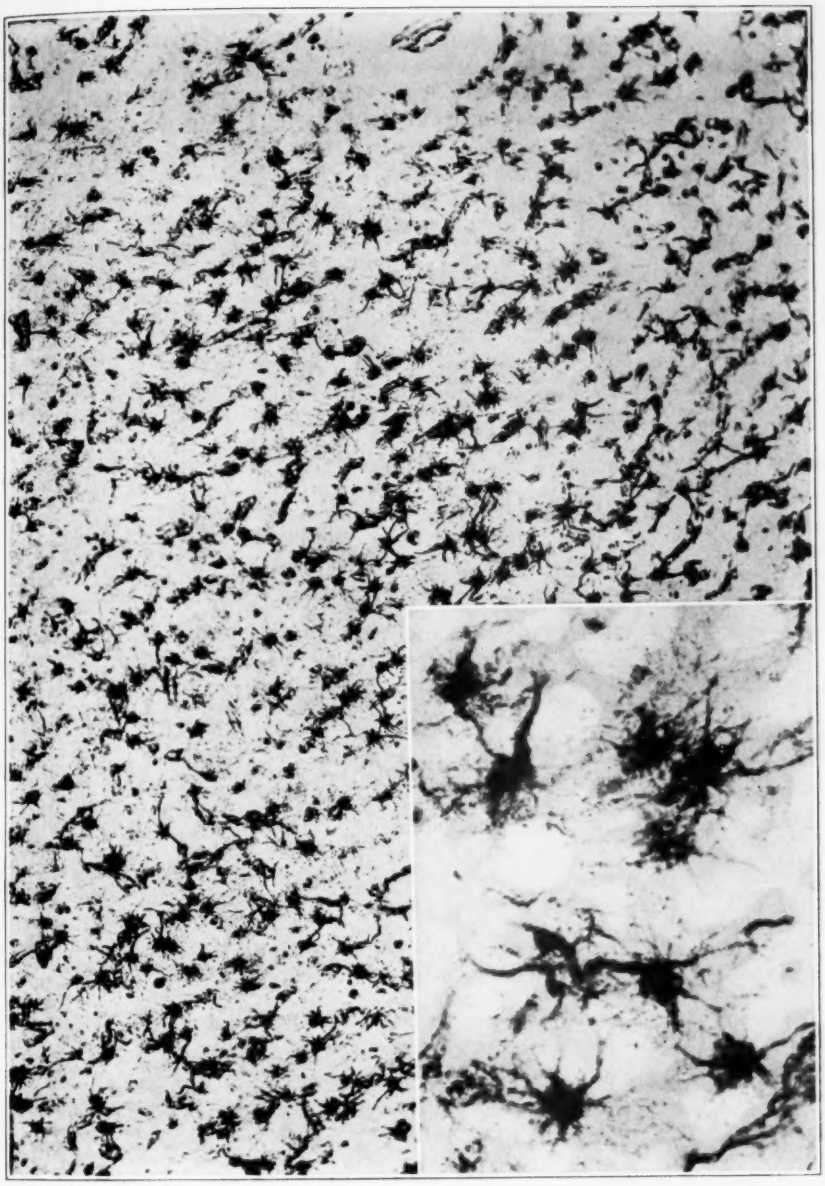

Fig. 15.—Photomicrograph of a section of an orbital convolution, showing the reaction of the cellular glia. In the insert both hypertrophy and beginning degeneration of the glial cells are seen with higher magnification. Cajal's gold sublimate stain.

cells extended to other layers. In a few zones the process of gliosis was lacking altogether, and the section appeared as poorly stained, with only remnants of nerve cells.

With the gold impregnation method of Cajal progressive changes were detected, including both hypertrophy and hyperplasia of astrocytes, together with slight degenerative changes (fig. 15). The Spielmeyer and the Holzer method revealed a correlation between demyelinization and glial proliferation in the white substance (fig. 16). Hortega's method failed to show a reaction of the microglia

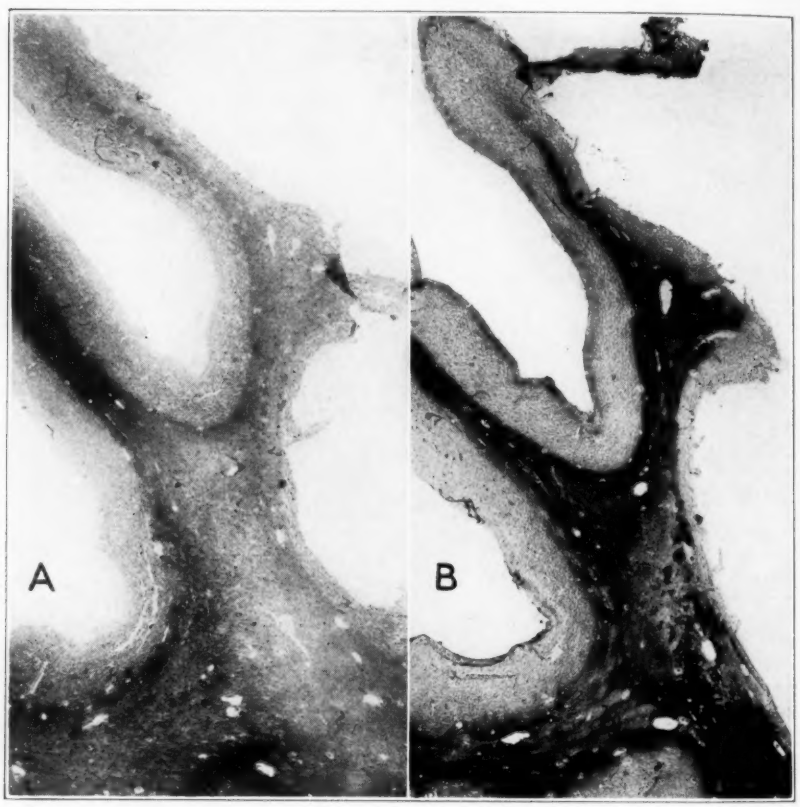

Fig. 16.—Photomicrograph of a section of the temporal lobe, illustrating the correlation between (*A*) demyelinization (Spielmeyer's stain) and (*B*) glial proliferation (Holzer's stain for glia).

and oligodendroglia. In only a few instances were hypertrophic changes observed involving the microglia cells; in addition, hyperplasia of oligodendroglia was seen in atrophic areas of the white matter.

Typical arteriosclerotic changes of the blood vessels were absent. There was, however, thickening of the adventitial connective tissue in some capillaries, suggesting the picture of capillary fibrosis. In addition, many small cortical blood vessels showed proliferative changes in the sense of active mitosis and multiplication of the inner lining cells, thus leading to a certain degree of endarteritis. Only

occasionally were hyaline degenerative changes encountered. No inflammatory changes of any sort were observed in the parenchyma or the meninges or surrounding the blood vessels.

Turnbull's method for iron pigment disclosed a considerable amount of iron, particularly in the third temporal convolution of each side, where a diffuse blue stain of the white matter was present at its boundary with the gray matter. In addition, granular iron pigment was seen in both the gray and the white matter surrounding the blood vessels or free in the tissue or embedded in all types of cellular elements, particularly oligodendroglia cells. The second and fifth cortical layers seemed to show a higher percentage of iron granules. A certain parallelism existed between the amount of iron pigment and the degree of the atrophic process.

In the basal ganglia, particularly in the caudate nucleus, atrophic cellular changes of the same type as those in the cortex were seen; a considerable amount of iron pigment was also detected. The thalamus showed a certain amount of atrophy. In the external and extreme capsules a particularly intense gliosis of isomorphic type was shown by Holzer's method. The ependymal lining cells of the ventricles showed proliferation, with occasional formation of very small cysts.

In the cerebellum, Bielschowsky's method showed senile lesions consisting of thickening and an increase in the argentophilia of the pericellular network and the dendrites of the Purkinje cells. The axis-cylinders occasionally showed ball-like or elliptic swellings with pronounced argentophilic reaction, the so-called torpedos (Bouman). Spielmeyer's method disclosed slight rarefaction of myelin sheaths, particularly in the molecular layer. Demyelinization in small patches was occasionally present in the white substance. The cells of the dentate nucleus contained a considerable amount of yellow pigment, which was insoluble in xylene.

The pons, medulla and spinal cord failed to show pathologic changes.

Case 2.—*History.*—V. W., a white man aged 55, of Scottish extraction, a plumber, was admitted to the Rockland State Hospital on April 4, 1934.[17] There was no family history of mental or nervous disease. The patient, the oldest of five children, had always been healthy. He had had little education but was capable and successful in business. He was married and without children and was selfish and unaffectionate in his attitude toward his wife and relatives. He made friends easily but quarreled with them a great deal because of stubbornness, pride and instability.

In 1931, at the age of 51, the first mental symptoms were observed. Without apparent reason the patient became unattentive and more irritable than normal and was frequently confused in the accomplishment of performances, forgetting easily names and things to do. A year later he was forced into bankruptcy. It was then stated that his mental condition had contributed largely to the failure in business. Following this, although apparently worrying about financial difficulties, he spent money recklessly. His social and ethical behavior contrasted with his former attitude. He took baths with the door open, wandered around the house without clothes and was violent and obscene in his attitude toward friends. Whereas formerly he had led a vigorous sexual life, he became impotent.

In February 1933, he entered the New York State Psychiatric Institute and Hospital. The following clinical notes were made: "The patient was confused and disoriented, childish, unstable and irritable. He exhibited marked lability of affect and dilapidation of thinking capacity, attention and mental tension. His condition grew progressively worse; he became slovenly and extremely

17. The clinical record in this case was furnished by Dr. R. E. Blaisdell, superintendent of the Rockland State Hospital, Orangeburg, N. Y.

unstable, flew into a fury on little provocation, chuckled and laughed a good deal and had auditory hallucinations. On occasion he wet himself and thought this a huge joke." He was discharged in March 1934, with the diagnosis of psychosis associated with cerebral arteriosclerosis, and was transferred to the Bellevue Hospital.

The clinical notes at the Bellevue Hospital were as follows: "The patient laughed continually in a silly, empty manner. He talked in a monotonous way, sometimes repeating the examiner's question. Examination revealed defects of memory and confabulations. Marked disturbances in judgment were shown. He was untidy and careless and was disoriented for time and place."

Physical Examination.—On admission to the Rockland State Hospital the patient was well nourished and well developed, apparently 60 years of age. A moderate degree of peripheral arteriosclerosis was noted, while changes in the retinal vessels were scanty. Except for the sluggish reaction of the pupils and a certain unsteadiness in gait, the results of neurologic examination were normal.

Mental Examination.—The patient was restless and wandered about the ward, upsetting the furniture. He seemed considerably confused and disoriented. He had prolonged spells of laughter without apparent cause. On occasions he wet and soiled himself. During mental examination he cooperated poorly. He had marked paucity of ideas, and his remarks were irrelevant and disconnected. He showed a strong tendency to repeat whatever was said to him. Emotional reaction was markedly childish; he had periods of forced laughter during which he laughed heartily without real mirth, as though it were forced and uncontrolled. No definite delusions or hallucinations were elicited. Orientation was absent. Remote and recent memory were markedly impaired, and the patient confabulated freely. Retention and immediate recall, counting and calculation were extremely poor. He did not read, and his writing was unintelligible. School and general knowledge were poorly retained. Tests for thinking capacity and attention confirmed the profound intellectual deterioration. Insight was lacking. A tentative diagnosis of presenile psychosis, of the Alzheimer type, was made.

Course.—There was progressive intellectual dilapidation. Echolalic manifestations became more evident, and aphasic symptoms occurred, the exact nature of which could not be investigated because of the profound mental deterioration of the patient. In March 1935 there were signs of physical failure and in July 1935 death followed, with signs of cardiac decompensation. The duration of the disease was four years.

Gross Pathologic Observations.—Postmortem examination was performed eleven hours after death. Mild arteriosclerotic changes were present in the coronary vessels of the heart, and atheromatous plaques were scattered on the aortic valves. The liver was small and of nutmeg appearance. Otherwise examination of the various organs of the chest and abdomen gave normal results.

The brain weighed 1,040 Gm.; the pia was slightly adherent and thickened over the frontal lobes. On external examination the brain showed a marked atrophy limited to the prefrontal lobe and extending to the two anterior thirds of the three frontal convolutions and to the orbital gyri. The atrophy was more evident in the anterior portion, where the frontal pole appeared considerably shrunken. The other portions of the cortex had grossly a normal appearance, though the gyri gave the impression of being somewhat narrower than usual. On section the lateral ventricles were dilated, especially in the frontal horn, where the white matter was considerably shrunken.

Microscopic Examination.—Sections of various areas of the brain were studied with the same histologic methods as were used in case 1. A more detailed report of the observations in the prefrontal lobe follows, as the lesions there were typical from both the qualitative and the quantitative point of view.

In the prefrontal lobe Nissl's method showed marked destruction of nerve cells, which in numerous microscopic fields were reduced to a few distorted and shrunken elements. The various layers of the cortex were at times evenly involved; at other times preference of the lesions was shown for the superficial layers or, again, for the middle or inner layers. It was noteworthy that in numerous instances there were groups of better preserved nerve cells, which constituted cellular islands amid the sclerotic tissue. Altogether, the gross distribution of the lesions recalled that reported in case 1. The type of cellular destruction was that already described in case 1, but no ischemic type of reaction was seen. Pigmentary surcharge of the nerve cells and fatty degeneration were more marked than in case 1. In a few instances cellular swellings were encountered in the posterior portion of the prefrontal lobe, where the atrophy was less pronounced. The Bielschowsky stain confirmed the profound disintegration of the nerve parenchyma shown by Nissl's method, but no argentophilic bodies were detected in this region of the brain. Senile plaques and Alzheimer's neurofibrillary changes were likewise absent. Stains for myelin sheaths disclosed destruction of myelin paralleling the atrophy of the nerve cells; in the frontal pole the myelin was reduced to small fragments which were stained only faintly by hematoxylin. In these markedly atrophic regions the neuroglia reacted strikingly; in the Holzer preparations a dense marginal gliosis was seen, consisting of thick glial fibrils, irregularly interwoven; in other layers of the cortex glial cells were more numerous and were particularly well brought out by the Cajal method. This gliosis, although spreading all over the atrophic areas, was not evenly distributed, zones of intense overgrowth encroaching on zones of poorer glial reaction. As in case 1, the Hortega preparations showed that the microglia participated only slightly in the pathologic process. The blood vessels, which showed a certain degree of fibrosis and endarteritis, as already described in case 1, revealed no typical arteriosclerotic changes. With Turnbull's method a large amount of granules of iron pigment was spread evenly in both the gray and the white matter of the atrophic areas.

In areas other than the prefrontal lobe, microscopic examination showed diffuse lesions essentially similar to those in the prefrontal region, though much less pronounced. Cellular atrophy was seen in numerous cortical fields examined with the Nissl method, particularly in the temporal lobe. At times the lesions presented themselves in a laminar distribution, mainly in the superficial layers; at other times pictures of abrupt transition between markedly atrophic and almost normal areas were seen, together with acellular areas. This characteristic type of lesion has already been illustrated in case 1. It was noteworthy that the cellular changes were not uniformly distributed throughout the cortex and that the irregularity of lesions was a striking feature, even in individual microscopic fields. The same unevenness in distribution was observed in preparations stained for glia. In the parietal lobe, for instance, Holzer's stain showed small areas of gliosis irregularly distributed in both the gray and the white matter.

Cellular swellings were rare and irregularly scattered in groups of a few elements. A few argentophilic bodies were observed in Sommer's sector of the cornu ammonis; they were generally round or oval, but some showed bizarre configurations. Nowhere else were the argentophilic inclusions observed, in spite of

an extensive investigation with both the Bielschowsky and the Braunmühl method. The same methods failed to show senile plaques or Alzheimer's neurofibrillary changes.

Apart from a decrease in volume and an increase in the amount of iron pigment, the basal ganglia were normal. Microscopic examination of the cerebellum, medulla and spinal cord revealed practically normal structure.

In both cases intellectual deterioration dominated the clinical picture, whereas neurologic signs, in particular aphasic manifestations, occurred only in a late stage, when profound dementia precluded any careful psychologic investigation. A correct diagnosis was therefore missed. As a fact, in all cases the literature in which a correct clinical diagnosis was made (Kahn,[18] Stertz,[19] Urechia,[20] Schneider,[21] Lemke [22] and others) aphasic signs associated with a mental picture suggesting lesion of the frontal lobe were shown from the beginning. Even in the absence of neurologic signs, however, a deeper knowledge of the pathophysiologic activity of the frontal lobe may lead to a correct diagnosis on a purely psychologic basis, as was shown recently by Goldstein.[23] Encephalography, revealing localized atrophy of the brain, constituted an important diagnostic procedure; when performed (Bingel,[24] Bürger and Prinz,[25] Lemke,[22] Nichols and Weigner [14b] and Flügel [26]) it helped to shape the final diagnosis.

In case 2 in our series, two diagnoses were suggested: arteriosclerotic psychosis and Alzheimer's disease. The former possibility was later ruled out because of the scarcity of physical signs of vascular lesion and the absence of focal cortical symptoms of sudden onset. Moreover, instead of a lacunar type of intellectual impairment and relative integrity of the personality, such as are generally observed in asso-

18. Kahn, E.: Demonstration der präsenilen Verblödungsprozesse, Zentralbl. f. d. ges. Neurol. u. Psychiat. **40**:733, 1925.

19. Stertz, G.: Ueber die Picksche Atrophie, Ztschr. f. d. ges. Neurol. u. Psychiat. **101**:729, 1926.

20. Urechia, C. J.: Contribution à l'étude de la maladie de Pick, Encéphale **25**:728, 1930.

21. Schneider, C.: Ueber die Picksche Krankheit, Monatschr. f. Psychiat. u. Neurol. **65**:230, 1927.

22. Lemke, R.: Ein Beitrag zum Krankheitsbild der Pickschen Atropie, Arch. f. Psychiat. **101**:623, 1934.

23. Goldstein, K., and Katz, S. E.: The Psychopathology of Pick's Disease, Arch. Neurol. & Psychiat., to be published.

24. Bingel, A.: Ueber die Picksche Atrophie, Zentralbl. f. d. ges. Neurol. u. Psychiat. **63**:830, 1932.

25. Bürger and Prinz: Klinik des Beginns der Pickschen Atrophie, Deutsche med. Wchnschr. **59**:594, 1933.

26. Flügel, F.: Die Encephalographie als neurologische Untersuchungsmethode, Ergebn. f. inn. Med. u. Kinderh. **44**:327, 1932.

ciation with arteriosclerotic psychosis, the patient presented profound mental deterioration, with complete disintegration of personality. Clinical differentiation from Alzheimer's disease was probably impossible without the aid of an encephalogram; the patient showed, in fact, symptoms such as hallucinatory experiences, delusions and confabulations which are exceptional in Pick's disease and are more characteristic of Alzheimer's disease. This case illustrates once more the difficulty of clinical differentiation of Alzheimer's and Pick's disease. In the two conditions the ages and the slowly progressive courses are the same, and the types of intellectual and emotional impairment are similar. The following points may help in diagnosis: In Alzheimer's disease a certain degree of anxiety and depression is more frequently observed, and the defect of memory is more severe, involving all processes of memory —reception, retention and reproduction. In Pick's disease retention and reproduction of old engrams may be demonstrated even in advanced stages. According to Stertz,[19] the mental symptomatology in Alzheimer's disease is due mainly to disorders of memory; even some elements of the asymbolic apraxic and aphasic syndrome may be attributed to defects in memory. Moreover, in Alzheimer's disease, palilalia, iterations and logoklonia are frequent, whereas in Pick's disease they do not occur. Logoklonia particularly has been considered as characteristic of Alzheimer's disease, whereas echolalic phenomena are more characteristic of Pick's disease. Finally, in Alzheimer's disease epileptic seizures are frequent, even in early stages; in Pick's atrophy they occur rarely, and only in an advanced period of the disease.

The pathologic condition in both the cases reported here was typical of Pick's disease, consisting of circumscribed cellular atrophy of the cerebral cortex, cellular swellings and argentophilic bodies. Senile plaques, Alzheimer's neurofibrillary changes and arteriosclerotic lesions were characteristically absent.

The first case was one of frontotemporal atrophy, the second, a typical instance of prefrontal localization. These two types are the most frequently encountered, the former constituting about 38 per cent and the latter 27 per cent of cases reported in the literature, while in 21 per cent the involvement was temporal. A few cases of combined fronto-occipital and temporo-occipital localization have been reported, whereas the existence of a pure occipital type (Pick,[1] Rosenfeld[27] and Horn and Stengel[28]) is doubtful.

27. Rosenfeld, M.: Die partielle Grosshirnatrophie, J. f. Psychol. u. Neurol. **14**:115, 1909.

28. Horn, L., and Stengel, E.: Zur Klinik und Pathologie der Pickschen Atrophie: Ueber die nosologische Stellung der "Pickschen Krankheit," Ztschr. f. d. ges. Neurol. u. Psychiat. **128**:673, 1930.

Detailed histologic examination showed that the atrophic lesions, with their accompanying manifestations, although markedly pronounced in the grossly atrophic areas, were diffuse throughout the entire cortex. The architectural alterations varied: Complete disorganization was seen in the most atrophic areas, and partial derangement, at times with a laminar distribution, was encountered in less atrophic areas. There was, however, no definite rule as to the distribution of the atrophy in the various architectural fields of cortical laminae, nor was there any uniformity in the glial reaction accompanying the destruction of nerve cells. In addition, there was evidence of tissue response to a vascular condition, as shown by perivascular acellular areas, patchy demyelinization and abrupt passages between markedly atrophic and almost normal zones. Intimately intermingled with this was a process of slow necrobiosis of the nerve cells, with thinning or gradual disappearance rather than active fragmentation and disintegration of both the myelin sheaths and the axis-cylinders. The same process seemed at times to affect also the glial tissue and to interfere with its reactive capacity. The absence of mobilization of microglia might be due either to the lack of considerable products of disintegration or to primary involvement of these cells, interfering with the phagocytic activities.

An analysis of the clinicopathologic observations on our material integrated with a study of the verified cases published in the literature has allowed us to reconsider the problem of the nature of Pick's disease and in particular the question whether the condition is to be classified with heredodegenerative diseases.

In our cases the family history was negative for mental disease, as it was in 80 per cent of cases reported in the literature. In cases in which the family history was reported as positive the mental heredity was dissimilar in character, the diseases most frequently recorded being alcoholism, cerebral arteriosclerosis and senile dementia. Of greater significance for this problem is the occurrence of Pick's disease in siblings. However, of the cases reported, only those of Grünthal [11] and Braunmühl and Leonhard [12] were irrefutable instances; in the other cases (Reich,[3] Verhaart [29] and Grünthal [30]) the diagnosis was questionable since control by pathologic examination was lacking. At present, therefore, the number of observations seems insufficient to corroborate on a genetic basis the heredodegenerative nature of the disease and its independence of senility. It should be noted, moreover, that recent studies have brought data in favor of a hereditary influence

29. Verhaart, W. J. C.: Over de ziekte van Pick, Nederl. tijdschr. v. geneesk. **74**:5586, 1930.

30. Grünthal, E.: Klinisch-genealogischer Nachweis von Erblichkeit bei Pickscher Krankheit, Ztschr. f. d. ges. Neurol. u. Psychiat. **136**:464, 1931.

in senile dementia (Meggendorfer [31] and Weinberger [32]). In particular, the observation on the occurrence of senile dementia in twins, published by Scheele,[33] detracts from the significance of the cases of Pick's disease in siblings.

More than genetic data, presumptive peculiarities of the pathologic process are stressed by supporters of the heredodegenerative nature of Pick's disease. Considerable attention has been paid first to the localization of the atrophic areas, and attempts have been made to establish that the pathologic process involves certain systems, in accordance with rules which govern the pathologic picture of heredodegenerative forms. Thus, it has been repeatedly claimed that there exists a relationship of the atrophic process to the associative zones of Flechsig, to certain cyto-architectonic areas of Brodmann and to phylogenetically recent portions of the neopallium. Pick's disease has accordingly been classified by Gans [10] in the group of forms of abiotrophy with elective cellular necrobiosis, a condition characterized by congenital weakness of phylogenetically recent systems.

In both our cases the evidence contradicts any such electivity of the atrophy. Even on macroscopic examination the cornu ammonis, the hippocampus and the gyrus fusiformis—formations which are phylogenetically old—appeared seriously involved in case 1, whereas a phylogenetically recent area, Broca's center, was spared in case 2. Histologic examination, moreover, confirmed that atrophic changes extended without order not only outside phylogenetic fields but beyond the boundaries of the various areas of Brodmann or the associative systems of Flechsig.

The theory of the systemic electivity of the atrophic process presented itself in a new light after the observations of the laminar distribution of the cortical atrophy in the superficial layers (Altmann [34]). Since the distinction between the superficial and the deep layers of the cortex has a functional significance, the former being related to receptive-correlating functions and the latter to corticofugal and commissural efferent functions (Ariëns Kappers [35]), Pick's disease would in this event represent an elective pathologic process involving the asso-

31. Meggendorfer, F.: Ueber die hereditäre Disposition zur Dementia senilis, Ztschr. f. d. ges. Neurol. u. Psychiat. **101**:387, 1926.

32. Weinberger, H.: Ueber die hereditäre Beziehungen der senilen Demenz, Ztschr. f. d. ges. Neurol. u. Psychiat. **106**:666, 1927.

33. Scheele, H.: Ueber ein konkordantes zweieiiges Zwillingspaar mit seniler Demenz, Ztschr. f. d. ges. Neurol. u. Psychiat. **144**:606, 1933.

34. Altmann, E.: Ueber umschriebene Gehirnatrophie des späteren Alters, Ztschr. f. d. ges. Neurol. u. Psychiat. **83**:610, 1923.

35. Ariëns Kappers, C. U.: The Development of the Cortex and the Functions of Its Layers, J. Ment. Sc. **77**:692, 1931.

ciative receptive cortical system. A still more strict interpretation of the laminar distribution of the atrophy in Pick's disease was offered by Martha Vogt.[36] According to this author the lesion begins in layer III_1 and then invades layers III_2 and III_3. Later it spreads to the second and to the fifth layer; the sixth layer is only slightly involved and the fourth and seventh layers are generally spared. The pathologic process, in other words, follows a series of regular and constant successions, thus constituting a striking instance of a eumonic type of pathoclisis in the sense of O. and C. Vogt.[37]

In our material a careful examination of various cortical areas showed marked unevenness of involvement of layers, even in the least atrophic regions, where the pathologic process was in its early stages, so that no regular succession could be established. Even a preference for the third layer and, in general, for the superficial layer was not constantly observed, and often involvement of almost all layers or of the inner layers alone could be detected.

Furthermore, the significance in Pick's disease of extracortical lesions has been stressed by supporters of the heredodegenerative theory of the disease by comparison with Huntington's chorea and cerebellar atrophy; they thus postulated primary involvement of the extracortical system. In case 1 the basal ganglia showed a certain degree of involvement by the atrophic process, but it could easily be considered of secondary character. The cerebellum was normal. In case 2 both the basal ganglia and the cerebellum appeared normal. These observations are in agreement with the data in the literature. Cases may be occasionally found in which severe involvement of the basal ganglia (Braunmühl [38] and van Bogaert [39]) was shown, but many others are reported in which no extracortical changes could be detected. From another aspect the involvement of the basal ganglia does not constitute an element corroborating the exclusion of Pick's disease from the group of senile conditions, since a part of the neurologic picture presented at advanced ages may be considered precisely as the expression of an extrapyramidal syndrome with its pathologic correlation in lesions of the basal ganglia (Critchley [40]).

---

36. Vogt, M.: Die Picksche Atrophie als Beispiel für die eumonische Form der Pathoclise, J. Psychol. u. Neurol. **36**:124, 1928.

37. Vogt, C., and Vogt, O.: Erkrankungen des Grosshirns im Lichte der Topistik, Pathoclise und Pathoarkitektonik, J. Psychol. u. Neurol. **28**:1, 1922.

38. von Braunmühl, A.: Ueber Stammganglienveränderungen bei Pickscher Krankheit, Ztschr. f. d. ges. Neurol. u. Psychiat. **124**:214, 1930.

39. van Bogaert, L.: Syndrome extrapyramidal au cours d'une malade de Pick, J. belge de neurol. et de psychiat. **34**:315, 1934.

40. Critchley, MacDonald: The Neurology of Old Age, Lancet **1**:1221, 1931.

Not only the distribution of the lesions but certain morphologic aspects of the nerve cells have been offered as indicating the heredodegenerative nature of Pick's disease. Thus, Richter [4] and Kufs [5] compared the cellular swelling in Pick's atrophy with the characteristic cellular lesions of familial amaurotic idiocy, the basic feature of both being acute swelling and subsequent shrinkage of the hyaloplasm. But the cellular swelling presents itself without any regularity in Pick's disease; swollen cells were numerous in case 1 in our series and rare in case 2, and in several cases which have been reported they were absent. Moreover, the swelling never reaches the extreme degree and the bizarre shapes so characteristic of the Tay-Sachs disease. It rather recalls the type of central neuritis described by A. Meyer, which would suggest an entirely different interpretation. Finally (Helfand [41]), swelling of the same type has been described in the Hallervorden-Spatz disease, the heredodegenerative nature of which is far from being established.

In conclusion, it appears from the study of our material that the conception of the heredodegenerative nature of Pick's disease contrasts with the clinicopathologic facts and so far is purely speculative. It would be sounder, at least for the time being, to consider the disease in relation to the process of senility, as was first suggested by Pick on the basis of the age of onset and the clinical aspects. Pathologic observations seem to corroborate the original conception of Pick; in fact, in the senile brain diffuse cellular atrophy is constantly present, particularly in the frontal and temporal regions (Critchley [40]). Similarly, in Pick's disease neuronal changes consist primarily of cellular atrophy extending to the whole cortex, with accentuation (marked, to be sure) in the frontal and temporal lobes. The cortical senile atrophy may at times be most evident in the third layer (Gellerstedt [42]), as is also observed in Pick's disease. Histopathologic details common to both senility and Pick's atrophy add further evidence to the similarity, among which are the frequency of pigmentary surcharge and fatty degeneration of the nerve cells, the presence of numerous corpora amylacea and torpedos and the large amount of iron. Alzheimer's fibrillary changes are lacking, but the formation of cellular argentophilic inclusions, characteristic of Pick's disease, may be due to a similar physicochemical process leading to the formation of argentophilic substance, which is commonly observed in association with senility, as

41. Helfand, Max: Mitteilung eines Falles von Hallervorden-Spatzscher Krankeit, Ztschr. f. d. ges. Neurol. u. Psychiat. **143**:794, 1933.

42. Gellerstedt, N.: Zur Kenntnis der Hirnveränderungen bei der normalen Alterinvolution, Uppsala, Almqvist & Wiksells Boktryckeri a. B., 1933.

recently claimed by Braunmühl.[43] Senile plaques, to be sure, were not observed in our cases. However, the significance of these formations as pathognomonic of senile processes is still uncertain; moreover, it should be noted that in several instances of Pick's disease senile plaques have been observed in greater or less numbers within or outside the atrophic areas (Altmann,[34] Kufs,[5] Springlova,[44] Braunmühl,[45] Verhaart,[29] Marcus,[46] Guiraud and Cannu,[47] Moyano,[48] Frets,[49] Austregesilo[50] and Ladame[51]).

In our cases one also finds evidence of histopathologic changes representing tissue response to vascular involvement, such as circumscribed areas of cellular atrophy, abrupt transitions between zones of relatively better preserved tissue and zones with severe cellular damage, patchy accumulations of glia cells, with perivascular distribution, and areas of patchy demyelinization. In striking contrast with these tissue changes, however, there were noted only slight alterations in the blood vessels, consisting mainly of fibrosis of a few capillaries and occasionally of endothelial proliferation.

Similar contrasts are frequent in the general pathologic changes of arteriosclerosis. Numerous authors have stressed the point that in arteriosclerosis the symptoms are not proportionate to the vascular lesions and have attempted therefore to explain the pathogenesis of arteriosclerotic symptoms on the basis of vasospasms, thus substituting a functional point of view for or associating it with a purely morphologic one. Spielmeyer has repeatedly explained conflicting evidence in the pathologic examination of the brain in cases of arteriosclerosis by stressing the importance of vasomotor factors in pathologic involve-

43. von Braunmühl, A.: Kolloidchemische Betrachtungsweise seniler und präseniler Gewebsveränderungen, Ztschr. f. d. ges. Neurol. u. Psychiat. **142**:1-54, 1932.

44. Springlova, M.: Picksche lobäre Atrophie, Zentralbl. f. d. ges. Neurol. u. Psychiat. **46**:135, 1927.

45. von Braunmühl, A.: Zur Histopathologie der umschriebenen Grosshirnrindenatrophie, Virchows Arch. f. path. Anat. **270**:448, 1928.

46. Marcus, H.: Stirnhirnatrophie, Hygiea **92**:893, 1930; abstr., Zentralbl. f. d. ges. Neurol. u. Psychiat. **59**:485, 1931.

47. Guiraud, M., and Cannu, Y.: Syndrome démentiel présénile, Ann. méd.-psychol. **90**:242, 1932.

48. Moyano, B.: Demencias preseniles: II. Atrofia de Pick, Arch. argent. de neurol. **7**:240, 1932.

49. Frets, G. P.: De linkzijdige atrophie van Pick, Nederl. tijdschr. v. geneesk. **77**:4261, 1933.

50. Austregesilo, A., Jr.: Umschriebene Picksche Gehirnatrophie, Ztschr. f. d. ges. Neurol. u. Psychiat. **143**:627, 1933.

51. Ladame, C.: Contribution à la topographie des lésions histologiques du cerveau senile, Schweiz. Arch. f. Neurol. u. Psychiat. **27**:301, 1931.

ment of the nervous system in general and in cerebral arteriosclerosis in particular. The proof of vasomotor innervation of the cerebral arteries, as recently given by Cobb, makes vascular spasm a much more reasonable theory than it was a few years ago, when vasomotor control of the cortical vessels was generally denied.

On the basis of the histopathologic observations in our cases, recalling the occurrence of changes related to vasospasm in other conditions, we assume that vasomotor factors of the aforementioned nature play a rôle in the pathogenesis of Pick's disease. This working hypothesis of vascular spasm can explain the occurrence of circumscribed zones of gross cortical atrophy as a result of repeated local vasospasms.

Whether angiospasm may more easily affect predisposed tissue—tissue precociously old, so to speak—we are not prepared to say. Though in our material we met with changes comparable to those associated with normal and pathologic senility, we cannot exclude in the pathogenesis of the disease the additional interplay of vasospasm with other factors as yet unknown. The angiospasm might be produced by disturbance of the colloidal equilibrium, which, according to Braunmühl,[43] is characteristic of senile and presenile conditions. It may also be due to metabolic toxic factors of undetermined origin which act through the mechanisms of vasospasm or independently of it.

SUMMARY

Two cases of Pick's disease are presented in their clinical and pathologic aspects.

The theory of the heredodegenerative character of Pick's disease is discussed and found to be lacking in support from both the clinical and the pathologic standpoint.

The view is presented that Pick's disease should be considered as a presenile condition in the pathogenesis of which angiospastic factors play an important though not an exclusive rôle.

Angiospasm is compatible with an apparent morphologic integrity of the blood vessels.

PICK'S DISEASE

A CLINICOPATHOLOGIC CONTRIBUTION

K. LÖWENBERG, M.D., ANN ARBOR, MICH.

In 1892 Arnold Pick [1] published his first observation on atrophy of the brain with focal lesions, which he interpreted as atypical senile dementia. In analyzing the syndrome he was mainly concerned in correlating the clinical picture with the localization of the lesions. The great significance of Pick's contribution was not recognized until later studies proved that the symptom complex originally outlined was in reality a disease entity.

The disease is rare, about fifty cases having been reported in the literature. In spite of recent studies clinical diagnosis remains difficult, but knowledge of the pathologic features has been considerably enlarged. Four new cases are reported here.

REPORT OF CASES

CASE 1.—Edna N., aged 47, married, the mother of six children, was admitted to the hospital on May 13, 1931. There were no known hereditary trends. She had had a colloid goiter and "choking spells" for the past several years. One year prior to her admission she began to act peculiarly. When she saw a small object she looked at it very intently. When anything was said to her she repeated it over and over. She continually jumped up from a rocking-chair and hastened to the kitchen, returning a few minutes later, only to repeat the procedure. On retiring, she talked at great length concerning relatives "out in the West." At times she treated her children roughly and seemed "to have lost her mind completely." Frequently she attempted to follow her husband when he left the house, but the children were usually able to persuade her to return. Gradually she became more and more disinterested in her surroundings. At this time she had two or three "fainting spells," in which she became "limp and white" and "jerking movements" were noted.

Physical Examination.—The thyroid was somewhat enlarged; all the other internal organs were essentially normal. The Kahn tests of the blood and spinal fluid gave negative reactions. The blood pressure was 126 systolic and 70 diastolic. The reaction of the spinal fluid was positive to the Pandy test and negative to the ammonium sulfate and colloidal gold tests; a count revealed 13 cells per cubic millimeter.

Neurologic examination was impossible because of the patient's resistiveness.

Mental Examination.—The patient was restless and did not reply to questions. Her conversation was restricted to stereotyped muttering of "boys; girls; poison"

From the laboratory of Neuropathology of the State Psychopathic Hospital, the University of Michigan Medical School.

1. Pick, A.: Beiträge zur Pathologie und pathologischen Anatomie des Centralnervensystems, mit Bemerkungen zur normalen Anatomie desselben, Berlin, S. Karger, 1898.

and frequent hissing sounds. She clasped her throat occasionally as though she had a choking sensation. When an attempt was made to examine the heart action she became playful and resistive, made defensive movements and laughed in a silly way. She showed her tongue after repeated commands. When asked to shake hands she paid no attention, and when her hand was grasped she quickly pulled it away. She looked around the room and appeared alert, and it was easy to attract her attention by clapping or flashing a light. Occasionally she looked at certain objects with an inquiring gaze and pointed at them. She walked rapidly, usually following another person.

Course of Illness.—For several months the condition continued unchanged; the patient remained active and restless. Frequently she suddenly jumped out of bed and ran about the room. Her movements were quick and impulsive. She was practically mute; she emitted only the sound "sh-sh" and repeated constantly the phrase "boys and girls." It was impossible to establish any rapport with her. She did not pay any attention to her surroundings but kept herself neat.

Approximately three fourths of a year after her admission to the hospital her condition began to decline. The restlessness continued, but the movements became clumsy, and she fell several times, causing fractures of the wrist and hip. These fractures united without complications. Deterioration increased, and she became untidy.

In the fall of 1933 deterioration was advanced. She spent the day sitting in a chair, disinterested, passive, quiet and untidy. There was loss of weight. Examination at that time disclosed no evidence of a somatic disorder. During the six months prior to death the appetite became poor; she refused to eat and had to be fed. Death occurred on March 8, 1934, approximately four years after the onset of symptoms.

Clinical Summary.—A white woman, aged 47, descendant of an apparently healthy family, showed mental symptoms approximately one year prior to hospitalization. She became restless, repeated the same words continually and became unable to do the housework. In the hospital she was restless, but her movements became clumsy in the advanced stages of the disease, resulting in falls and fractures. Speech was greatly diminished, and she deteriorated rapidly.

The last stage of the disease was characterized by muteness, deep deterioration and complete inactivity. Failing appetite caused rapid loss of weight. Death occurred approximately four years after the onset of the symptoms.

Gross Pathologic Observations.—The brain weighed 850 Gm. and was asymmetrical, the right hemisphere being smaller than the left (fig. 1). The leptomeninges were thickened over both convexities. All visible vessels were delicate. Focal atrophy was present bilaterally in the frontal and temporal lobes, the insula and the region of the right gyrus marginalis (figs. 1, 2, 3 and 4). All other regions of the brain showed moderate diffuse atrophy.

Frontal Lobes: On both sides the atrophy terminated abruptly in the region of the sulcus praecentralis, affecting the anterior crest but sparing the posterior (figs. 1 and 2). An individual description of the frontal lobes is necessary, since the right lobe showed a more advanced stage of atrophy.

Right frontal lobe: On the convexity all the frontal gyri showed severe uniform atrophy (figs. 1 and 3). The convolutional crests of both frontal sulci and those of the horizontal, ascending and posterior rami of the sylvian fissure were very thin ("knife-blade atrophy" of German authors), and the sulci were deep and gaping (figs. 1, 2 and 3).

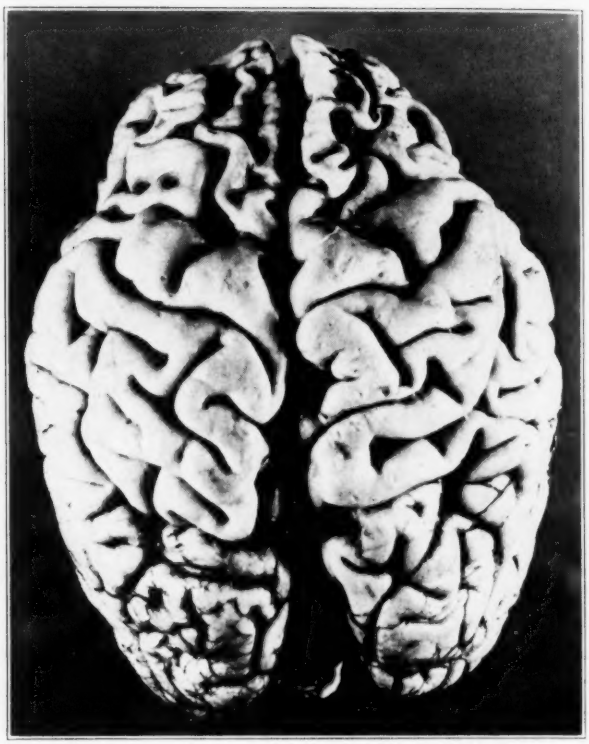

Fig. 1 (case 1).—Photograph of the brain showing atrophy of both frontal lobes, terminating bilaterally in the region of the right sulcus precentralis. The right hemisphere is slightly smaller and the right frontal lobe is more severely atrophic than the left.

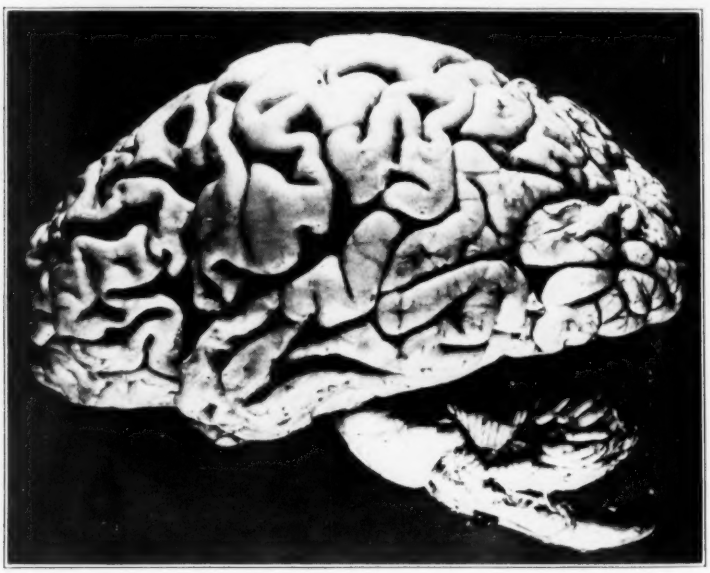

Fig. 2 (case 1).—Photograph of the lateral aspect of the brain, showing severe atrophy of the left frontal lobe, abruptly terminating in the region of the left sulcus precentralis. Severe atrophy of the anterior one half of the temporal lobe and moderate diffuse atrophy of the parietal lobe are evident.

On the base the gyri orbitales and the gyrus rectus were distinctly atrophic, but the atrophy was less pronounced than that of the convexity.

On the median surface the atrophy involved the gyrus frontalis superior and the gyrus cinguli, reaching the anterior ascending ramus of the paracentral sulcus but sparing the paracentral lobe. The genu corporis callosi was atrophic (figs. 3 and 4).

Left frontal lobe: On the convexity the gyri frontales superior and inferior showed advanced atrophy. The gyrus frontalis medius was better preserved (figs. 1, 2 and 3).

On the base the atrophy corresponded to that of the same area on the right side.

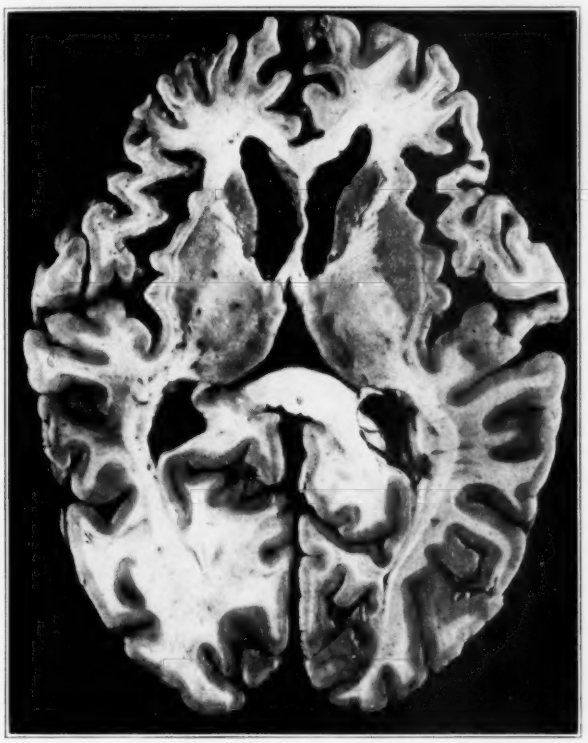

Fig. 3.—Photograph of a horizontal section of the brain, showing severe atrophy of the corpus callosum (genu) and the median surface of the frontal lobe, the operculum and the island on both sides. The right frontal lobe is more severely atrophic. The sides are reversed in the picture.

On the median surface the atrophy corresponded to that of the same area on the right side (figs. 3 and 4).

Temporal Lobes: Right: The atrophy was more pronounced on this side than on the left. On the convexity all three gyri showed advanced atrophy, the most severe damage being at the tip. The atrophy gradually diminished toward the gyri occipitales.

On the base the atrophy was less pronounced than on the convexity, being marked in the gyrus temporalis inferior, moderate in the gyrus fusiformis and

slight in the gyrus hippocampi. The change was restricted to the anterior half of the lobe.

Left: On the convexity the anterior halves of all three gyri were involved, the tip of the lobe being the most severely damaged (fig. 2).

On the base the anterior thirds of the gyrus temporalis inferior and gyrus fusiformis were moderately atrophic, while the uncus and the gyrus hippocampi were better preserved.

Parietal Lobes: The right lobe did not show appreciable atrophy except in the gyrus supramarginalis, where the change was moderately advanced (fig. 1). The left lobe showed moderate diffuse atrophy (figs. 1 and 3).

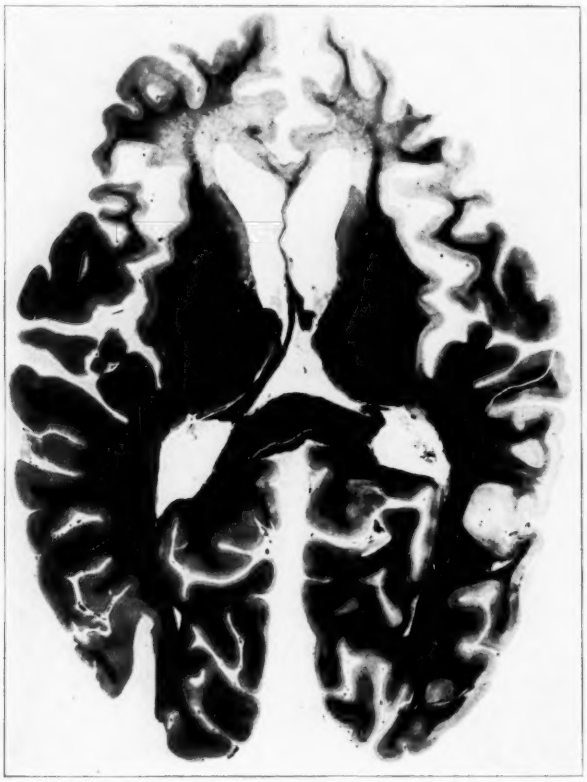

Fig. 4.—Photograph of a horizontal section of the brain, showing severe atrophy and demyelinization of the corpus callosum (genu) and the frontal lobe, anterior part of the operculum and island on both sides. Weigert-Kultschitzky stain; reduced one-half.

Occipital Lobes: There was mild general atrophy (figs. 1, 2, 3 and 4).

Horizontal Sections: The more severe involvement of the right side was particularly impressive in the anterior third of the right frontal lobe (fig. 3). The frontal area of the operculum and the insula showed advanced bilateral atrophy. The claustrum, capsula externa and capsula interna and the basal ganglia were well preserved. The genu corporis callosi was severely atrophic. The lateral ventricles

were moderately enlarged (fig. 3). In the atrophic areas both the gray and the white matter were very narrow, but the unstained material suggested that a considerable amount of myelin was still preserved (fig. 3).

Sections stained by the Weigert method revealed many additional details not visible in unstained material and demonstrated that demyelinization was much more advanced than had previously been suspected (fig. 4). The demyelinated areas were not entirely devoid of myelin and stained gray or gray-black. The myelin of the convolutional crests was not as severely damaged as that of the deeper layers. The corona radiata remained faintly visible on both sides. The convolutions of the median surface contained much less myelin than those of the convexity, but this condition varied in different sections. The demyelinization of the operculum and insula was severe in the anterior convolutions but diminished gradually in the posterior convolutions (fig. 4). Demyelinization of the temporal lobes was pronounced in the tips, the uncus and the cornu ammonis. The left lingual gyrus (not shown in the picture) was severely demyelinated.

The cortical myelo-architecture was greatly changed throughout both hemispheres, the destruction being most pronounced in the frontal and temporal areas. The tangential fibers were practically absent, and the radial fibers were reduced to short fragments.

The basal ganglia showed little change. The amount of myelin was slightly reduced in the caudate nucleus. The putamen, pallidum and capsula interna appeared normal. In the capsula externa and capsula extrema the myelin was distinctly reduced. There were no definite changes in the brain stem.

Histologic Observations.—Cortex: In the atrophic areas all layers of the cortex showed great loss of neurons, resulting in diffuse rarefaction of the cytoarchitecture. There was no outspoken status spongiosus (fig. 5).

The changes in the neurons were of two types: 1. Cell inflation: This is to some extent characteristic of Pick's disease. In these elements the cytoplasm was swollen; it stained pinkish blue or violet with thionine and contained no tigroid material. The nucleus was eccentrically placed and stained poorly in some of the cells.

2. Nonspecific shrinkage: The cells were markedly decreased in size and stained a homogeneous deep blue, showing no intracellular structure.

In sections impregnated with silver some of the neurons showed argentophilic inclusions, which appeared as amorphous black masses, frequently larger than the nucleus. Senile plaques and fiber changes of the Alzheimer type were absent.

The blood vessel system was normal. There were occasionally pigment-laden polyblasts in the adventitia. The number of axis-cylinders was greatly reduced in the atrophic areas. Sections stained by the Holzer method demonstrated a dense network of glial fibers and numerous astrocytes in the gray and white matter. Lipoids were observed in negligible amounts in some of the neurons and perivascular spaces. A diffuse reaction for iron was present in the cortex and in the white matter of the atrophic areas, but there was no iron in the glial cells.

Basal Ganglia: In the caudate nucleus and putamen the number of neurons was not reduced, but many of the cells were of the inflated type, and there were numerous argentophilic inclusions. The thalamus and pallidum contained a few shrunken neurons but were otherwise free from changes.

Brain Stem and Pons: No definite pathologic structure was shown.

Cerebellum: There was pronounced atrophy of the cortex of both lobi quadrangulares, parts of the lobi semilunares and the vermis. The myelin of the atrophic convolutions was greatly affected, but not all components of the myeloarchitecture shared equally in the loss. The plexus supragranularis, especially its

tangential fibers, was well preserved. Demyelinization was pronounced in the plexus intragranularis, its normally dense network of fibers being reduced to a few rarefied myelin sheaths. The structure of the central myelin cones varied greatly, some being severely affected while others showed only moderate changes. The white matter of the hemispheres was normal.

Sections stained by the Nissl method showed that the atrophy was not evenly distributed. Some of the convolutions were atrophic in their entirety, while others showed only partial degeneration (fig. 6). The molecular layer of such convolutions was markedly atrophic, being reduced to about one fourth of its normal width. Purkinje elements were reduced to a few cells, and the granular layer was greatly rarefied (fig. 6). Production of fibers was limited, and there was

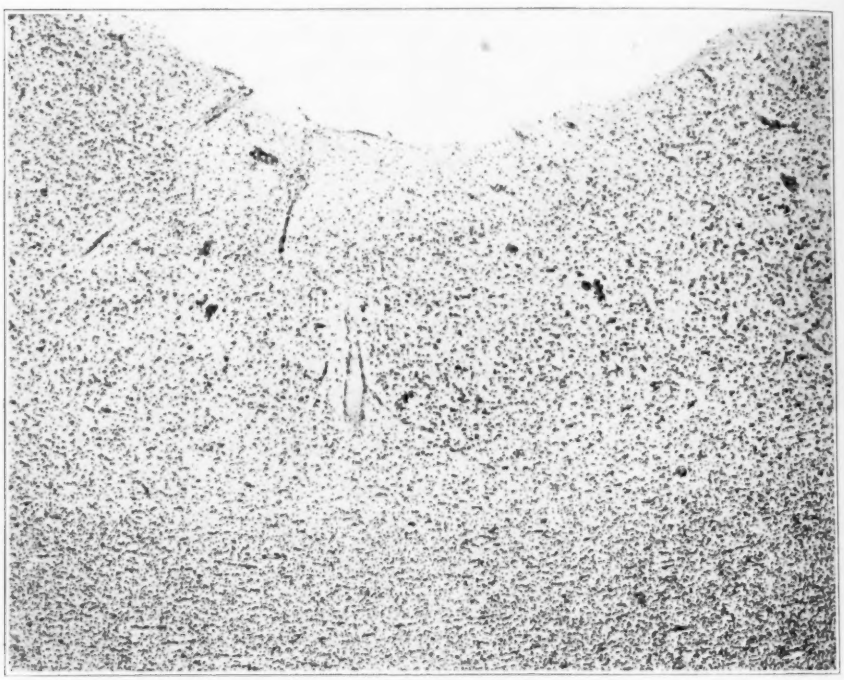

Fig. 5 (case 1).—Photomicrograph (Zeiss planar lens, 20 mm.) of a section of the cortex, showing diffuse rarefaction of the cyto-architecture. There is no spongy state. Van Gieson stain.

no glial cellular activity. The neurons of the dentate nucleus were well preserved. In the white matter of both cerebellar hemispheres glial fibers were abundant.

Case 2.—Dr. X., white, aged 65, was admitted to the hospital on March 15, 1923, because of disturbance of memory and change of personality. His father had died in the seventh decade of life, of cerebral arteriosclerosis; otherwise the family history was unimportant. Two years prior to his admission the family noted failure of memory, inability to converse and limitation of interests. He became careless in habits, and on one occasion he was discovered standing before a bookcase, apparently reading a book, and voiding on the floor. When reprimanded, he was surprised but not ashamed. He acquired also the habit of continually humming and singing.

One year prior to his admission he saw no patients and spent his time wandering about the neighborhood, visiting drug stores and news-stands. He spent hours in these places reading the literature and made himself a nuisance. He became indifferent to his family but manifested no irritability. He was brought to the hospital as a voluntary patient, accepting the situation passively and without emotion.

Physical Examination.—This revealed no somatic changes. The neurologic status was normal. The Wassermann reaction of the blood was negative.

Mental Status.—The patient showed no emotional reaction to the change of environment. He recognized his physician (whom he had known before), stating

Fig. 6 (case 1).—Photomicrograph of a section of the cerebellum, showing a partial degeneration of the convolutions of the cerebellum. Nissl stain; Zeiss planar lens, 20 mm.

that he had known the doctor for many years and correctly recalling previous occurrences. During the interview he sat with an unlighted pipe in his hand, sometimes putting it to his mouth. Later in the evening he became noisy, singing in a loud voice, and was awake most of the night.

Next morning he greeted the physician affably and was ready to go on ward rounds clad in a bath-robe. He was easily dissuaded from this and walked away singing loudly.

Course of Illness.—In the following six months the condition remained essentially the same. Occasionally he talked about his family and happy married life but showed no signs of emotion. At times he spoke of his early professional experiences, stating correctly that he had worked in this hospital shortly after

graduation. His manner was courteous and polite, and he caused no disturbance except for periods of loud singing. Once he went to sleep in a chair and, when reminded that it was getting late, remarked: "Well, I am a damn fool; I didn't know enough to go to bed. I was out here for observation, and I guess I am in the right place." In general, however, there was lack of insight into his mental state; he did not believe that it was necessary for him to be in a hospital but agreed that he should no longer practice his profession owing to his "advancing age." Otherwise he never referred to himself and was not concerned with his condition. His conversations many times were concluded with the remark: "Well, I think I will call upon Dr. C. (the medical director) tonight; I think I will go up and have a visit with the staff." He was usually easily pacified, however, and accepted any explanation without argument.

One year after his admission he appeared dull and increasingly forgetful, but he remained oriented and showed no mental clouding. Occasionally he accompanied the physician on the ward walks and enjoyed passing through the wards, without taking any particular interest in the patients. On one occasion he was confronted with one of his former patients, whom he recognized and with whose condition he seemed conversant. He remembered well the topography of the institution. In speaking of old experiences he displayed no emotional feeling. When questioned regarding the reason for being in the hospital he replied: "I suppose it's my damn-fool singing; it is a damn-fool thing, isn't it?" When asked why he indulged in singing, he was unable to give an explanation except to say that it had always been his custom to hum and sing at his office and at home. When informed of the serious illness of his wife he showed no interest.

During the second year of hospitalization mental failure became more rapidly progressive. The mental activities became more restricted; his interests waned gradually, and his memory began to fail rapidly. He was no longer able to dress himself and after receiving a bath often went to his room and sat on the edge of the bed in a bath-robe for hours unless he was directed to put on his clothes and was assisted in doing so. He was fairly tidy, but if a receptacle was not in his room he voided on the floor. His physical condition remained good, and there was no loss in weight.

The mental deterioration was far advanced two years after his admission. His activities grew more restricted from week to week, and passing events meant less and less to him. Signs of beginning physical decline appeared. He retired early in the evening and, unless special care was given, was untidy. On one instance he choked at dinner and became unconscious. Four pieces of meat were removed from his throat, but he did not regain consciousness for several hours. He gave up reading and rarely mentioned his old acquaintances and associations; he often spent hours singing "Old King Cole."

Several months prior to death he was greatly deteriorated, and it was not possible to communicate with him. The mention of old acquaintances or childhood associations brought no reaction. He was indifferent to his son's visits and usually misidentified him. The physical condition failed so rapidly and he became so untidy that it was necessary to keep him in bed.

In the last few weeks prior to death he lay in bed quietly, the facies expressionless and the mouth partially opened. Death occurred on Nov. 27, 1926, approximately six years after the onset of symptoms.

Clinical Summary.—A white man aged 65 presented loss of memory, perception and sense of propriety. At the time of his admission, two years after the onset of the disease, he was oriented, and memory for past events was good, but reten-

tive memory was poor. He had little insight; his interests were superficial, and he displayed no emotional reactions. His physical health was good. The clinical course was characterized by slow but steady mental decline. Toward the end he was deteriorated and became untidy. During the last weeks he was helpless and bedridden. The duration of the disease was approximately six years.

Gross Pathologic Observations.—The brain weighed 950 Gm. and was asymmetrical, the right hemisphere being smaller than the left. The frontal and temporal lobes on both sides showed advanced atrophy, more so on the right (fig. 7). The leptomeninges were thickened over both convexities, and the basal vessels were moderately sclerosed. All the other regions of the brain showed moderate diffuse atrophy.

Frontal Lobes: On both sides the atrophy terminated abruptly in the region of the sulcus praecentralis, affecting its anterior crest but sparing the posterior (fig. 7).

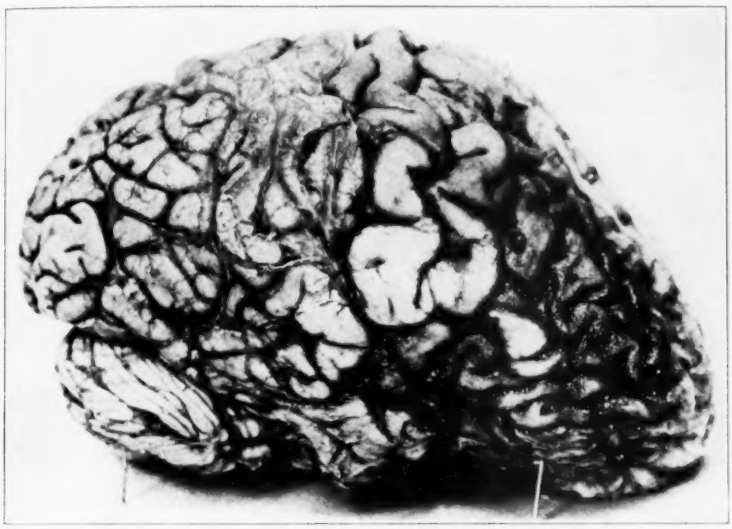

Fig. 7.—Photograph of the lateral aspect of the brain, showing severe atrophy of the right frontal and right temporal lobe. The frontal atrophy terminates abruptly in the region of the precentral sulcus.

Right lobe: On the convexity the atrophy involved all the frontal gyri; the crests of both frontal convolutions were thin and the sulci deep. The horizontal, ascending and posterior rami of the sylvian fissure were involved in the atrophy (fig. 7).

On the base the gyri orbitales and the gyrus rectus were atrophic, the change disappearing gradually toward the trigonum olfactorium. The atrophy was less severe than on the convexity.

On the median surface the anterior one half of the gyrus frontalis superior was atrophic, the atrophy disappearing gradually toward the sulcus paracentralis.

Left lobe: The atrophy of the convexity, base and median surface corresponded in extent with that of the same areas of the right lobe but was of milder degree.

Temporal Lobes: Right lobe: On the convexity all the temporal gyri showed pronounced atrophy, the tip of the lobe being particularly affected (fig. 7).

On the base the anterior halves of the gyrus temporalis inferior and gyrus fusiformis were severely atrophic; the gyrus hippocampi was atrophic to a lesser degree.

Left lobe: The atrophy corresponded with that of the right temporal lobe.

Parietal and Occipital Lobes: There was diffuse moderate atrophy.

The pons, medulla and cerebellum showed normal outlines.

Sections Stained by the Weigert Method: The asymmetry of the hemispheres was distinctly visualized in these sections (fig. 8). It could be recognized that

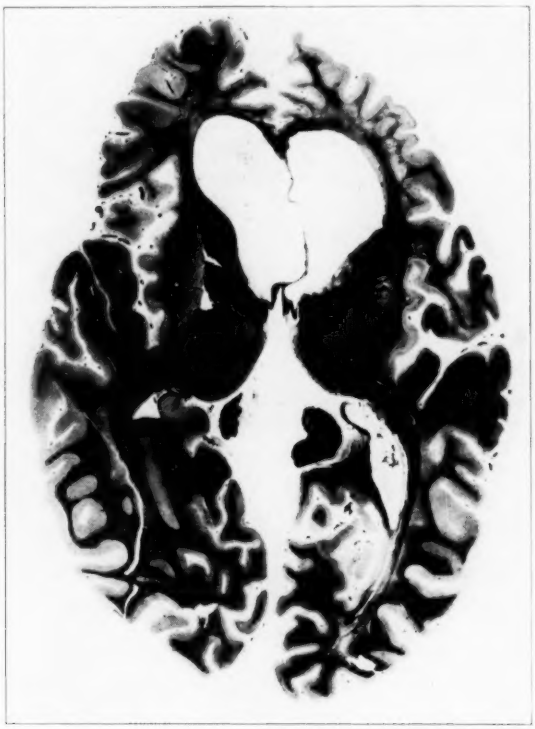

Fig. 8.—Photograph of a horizontal section, showing demyelinization of the frontal lobe, the anterior part of the operculum and the island on both sides and the right optic striation and right lingual lobe. Hydrocephalus internus is present. Weigert-Kultschitzky stain.

the atrophy was the result of reduction of both the gray and the white matter. The ventricles were greatly enlarged.

Right frontal lobe: The white matter was greatly reduced in the anterior part of the lobe and in the frontal part of the operculum. The corona radiata was poorly preserved, and the genu corporis callosi was atrophic. The gray matter was narrow (fig. 8).

Left frontal lobe: Destruction of the white matter, including the frontal part of the operculum, was less severe, and there was an island of preserved myelin in the tip of the lobe (fig. 8).

In the island of Reil on both sides the atrophy was much more pronounced in the three anterior gyri breves (fig. 8).

Temporal lobes: In both lobes the myelin was well preserved in the gyrus temporalis superior and greatly reduced in the gyrus temporalis medius.

The splenium corporis callosi was well preserved, and the cornu ammonis was moderately demyelinated.

Basal ganglia: The caudate body appeared narrow, and its myelin content and that of the putamen were greatly reduced. The capsula interna, thalamus and pallidum did not appear shrunken, but their myelin was moderately diminished.

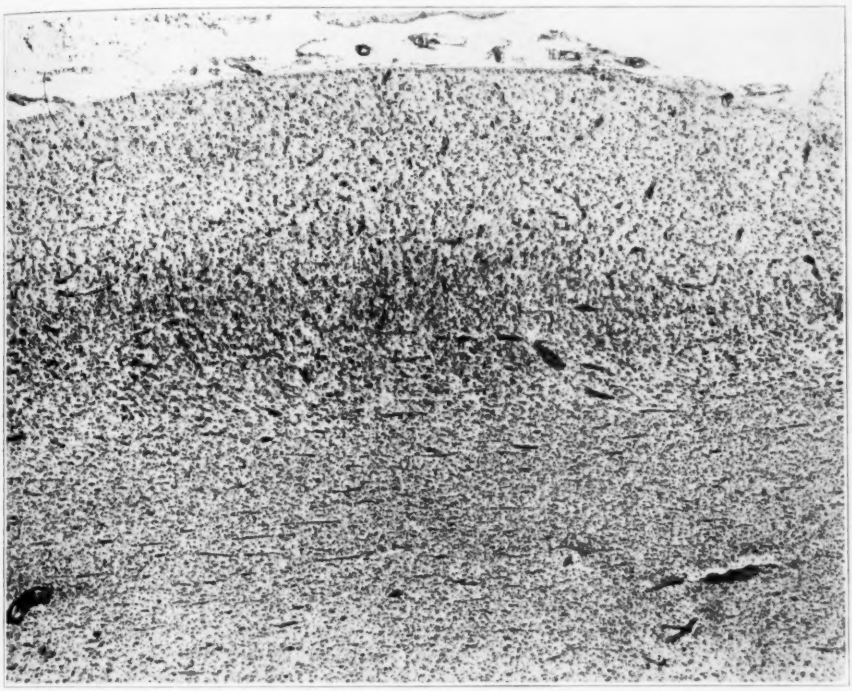

Fig. 9 (case 2).—Photomicrograph (Zeiss planar lens, 20 mm.) of the cortex, showing degeneration and status spongiosus of the third layer; layers IV to VI are very narrow. Van Gieson stain.

Occipital lobes: The optic striation was greatly demyelinated on the right and well preserved on the left, and there was an area of demyelinization in the right gyrus lingualis (fig. 8).

The myelo-architecture was destroyed in the frontal and temporal lobes and in the island on both sides. It was preserved in the parietal and occipital lobes.

Histologic Observations.—The cyto-architectural changes could be subdivided into three groups:

I. Areas in which the upper layers (layers II and III a) were affected. The second layer contained practically no neurons, and layer III a was considerably rarefied; layers IV, V and VI were better preserved but nowhere appeared entirely normal (fig. 9).

2. Areas in which layers II, III, V and VI were destroyed, the architecture being represented by a narrow and rarefied layer IV.

3. Areas in which all layers shared equally in the loss, causing considerable shrinkage of the cortex.

There was a widespread spongy state in the upper layers (layers II and III) of the atrophic areas, associated with microglial and macroglial activity and production of glial fibers in the limiting membrane. The blood vessels showed no changes, and there was no evidence of arteriosclerosis.

In spite of far advanced degeneration there was no inflation of cells, the neurons appearing greatly shrunken. Argentophilic inclusions, senile plaques and Alzheimer fibers were absent. Lipoid deposits were restricted to scattered droplets in some of the perivascular spaces. The myelo-architecture was destroyed in the frontal and temporal lobes and the island on both sides. It was better preserved in the parietal and occipital lobes.

The aforementioned observations (with the exception of the spongy state) were not limited to the atrophic areas but could be seen in a lesser degree throughout the brain.

Basal Ganglia: The neurons were shrunken in the caudate nucleus and putamen and, to a lesser degree, in the pallidum and thalamus. There was moderate glial activity similar in type to that in the cortex.

The pons, medulla and cerebellum showed no definite changes.

The white substance was rich in nuclei and contained numerous astrocytes and atypical glia.

Case 3.—J. C., aged 64, who was admitted to the hospital on Dec. 6, 1907, had a personal history which was without significance. The family history revealed that one aunt died in a state hospital; her daughter was "peculiar," and one paternal cousin was a patient in a state hospital. The patient had nine brothers and one sister; nothing was known concerning their mental health.

In 1902, at the age of 59, the patient became forgetful, frequently lost his tools and repeated things over and over. Several times he went to a neighboring town to trim trees but, instead, spent several days in a hotel. On returning home he stated that he had trimmed trees but was unable to explain why he had no money. Several months before his admission he fell and was unconscious for a few minutes, but no convulsive movements were noted. After this he became very active and irritable. He imagined that he was doing many things. He went to the post-office several times a day, for no apparent reason, and was profane and restless, especially at night. At times he complained of dizzy spells, headache and unpleasant sensations in the abdomen.

Physical Examination.—This, including laboratory studies, revealed nothing abnormal.

Neurologic Examination.—The pupils were equal and reacted sluggishly to light; the patellar reflexes were unequal; the superficial reflexes were normal, and there was slight tremor of the hands.

Mental Examination.—On his admission the patient lay quietly in bed; he was amiable and interested in his surroundings. There was no articulatory defect. He understood questions but was disoriented. He designated the year as 1865 and did not know the name of the town. He did not realize that he was in a hospital and said: "I cannot think just now." He had no insight into his condition. His school knowledge and memory for past events were retained. There was no evidence of hallucinations or delusions.

Course of the Illness.—In the following months the patient became restless and wandered about the ward constantly. He wanted to go home and tried to open every door. Sometimes he stated that he had been in town and wandered up and down the streets. He remained good natured.

Approximately half a year after his admission he became less active and preferred to sit quietly in a chair, without taking any interest in reading or in his surroundings. When addressed he laughed and joked, saying that there was nothing cross about him but his name (Cross); however, there were periods of irritability lasting for a day or two. Memory became poor, and there was progressive mental deterioration. He was untidy at times.

One year after his admission a profound mental change was noted. He was frequently disturbed, walking up and down the hall and yelling: "Hay, straw; hay, straw," and singing obscene songs in a loud voice. He was confused and forgetful. When told to stop he was quiet for a while and then again became noisy. He was untidy.

In the fall of 1909, two years after his admission, he was greatly deteriorated and confused, and it became difficult to communicate with him. However, he still gave his age correctly.

In May 1910, six months prior to death, he fell suddenly and had a few tonic and clonic convulsive movements. He appeared confused after this but soon recovered. A week later there occurred another similar seizure, following which there was rapid physical decline. He died of diarrhea on Nov. 12, 1910.

Clinical Summary.—A man aged 64, with three instances of mental disease in the family, became forgetful and irritable at 59. Later there was slowly advancing deterioration, with restlessness, epileptiform seizures and complete deterioration and debility toward the end. Death occurred at the age of 67. The duration of the disease was approximately from eight to nine years.

Gross Pathologic Observations.—The brain weighed 1,250 Gm. and was asymmetrical, the right hemisphere being smaller than the left. Both the frontal and the temporal lobes were atrophic (fig. 10).

Right Frontal Lobe: On the convexity atrophy involved all three frontal gyri, terminating abruptly in the region of the precentral sulcus (fig. 10).

On the base the orbital gyri and the gyrus rectus showed an advanced stage of atrophy.

On the median surface the anterior half of the superior frontal gyrus and the gyrus cinguli were distinctly atrophic (fig. 11).

Left Frontal Lobe: On the convexity atrophy was restricted to the anterior two thirds of the superior frontal gyrus. The medial and inferior frontal gyri showed far less atrophy. Broca's area was slightly atrophic (fig. 10).

On the base the gyri orbitales and gyrus rectus showed less advanced atrophy than those on the right.

On the median surface the anterior thirds of the superior gyrus and gyrus cinguli showed a moderate degree of atrophy (fig. 11).

Right Temporal Lobe: On the convexity the superior and inferior temporal gyri showed a mild degree of atrophy; the median temporal gyrus was severely affected.

On the base there was slight diffuse atrophy of all the gyri.

The remaining areas of the brain showed moderate diffuse atrophy (fig. 10).

Sections Stained by the Weigert Method: This method revealed almost complete demyelinization of the frontal lobe, the anterior part of the operculum and the island on both sides and of the genu corporis callosi. The changes were more

pronounced on the right. The corpus caudatum and the putamen were narrow, and their myelin was reduced. The internal capsule and the thalamus were well preserved (fig. 11). The ventricles were greatly enlarged.

The myelo-architecture was destroyed in all the atrophic areas. The myelin was better preserved in the parietal and occipital lobes, without reaching its normal density.

Histologic Observations.—In the atrophic areas the first layer was of normal width but contained numerous astrocytes. Layer II was very narrow, and the neurons were shrunken and reduced in number. Layer III contained almost no

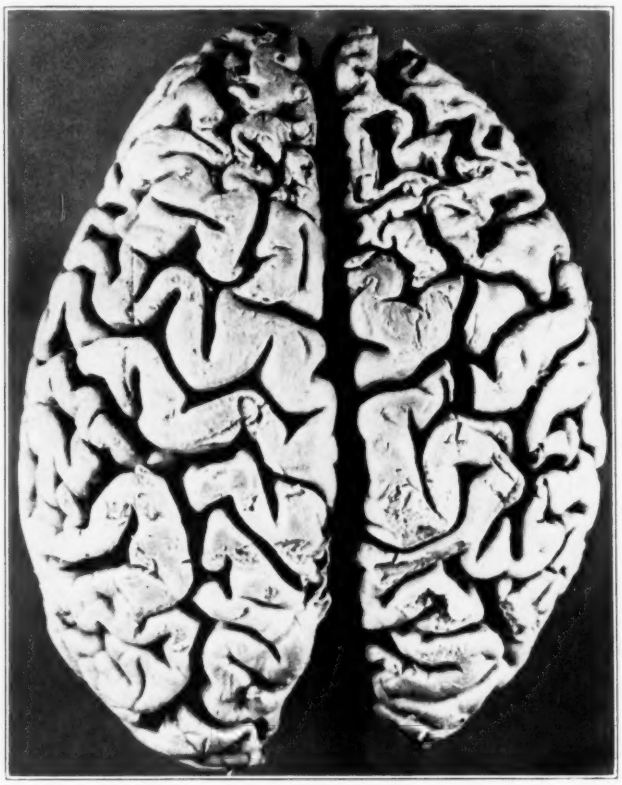

Fig. 10 (case 3).—Photograph of the dorsal surface of the brain, showing atrophy of the anterior half of both frontal lobes, more severe on the right.

neurons, and there was an outspoken spongy state. Layers IV, V and VI were narrow and poorly demarcated (fig. 12). The cells were shrunken and the cortex was extremely narrow. In the better preserved areas the architectural changes and the degeneration of the neurons were less marked, but moderate rarefaction of the third layer was a frequent occurrence.

The basal ganglia, brain stem, pons, medulla and cerebellum showed no definite pathologic changes.

Inflated neurons, senile plaques, fiber changes of the Alzheimer type and inclusion bodies were not observed. The number of axis-cylinders was greatly

reduced in the atrophic areas. The blood vessel system showed moderate arteriosclerotic changes. The white matter contained a dense network of glial fibers.

CASE 4.—Peter M., aged 24, a Negro, who was admitted to the hospital on Aug. 31, 1927, had no known relatives, and no family history was available.

Examination.—At the time of his admission the patient was described as negativistic, uncooperative, seclusive and withdrawn. He would not answer questions, and his speech was unintelligible. He murmured continually to himself, but no words could be understood. His facial expression was that of scowling perplexity. His eyes were open and followed a moving object. He obeyed commands slowly. He was untidy and incontinent.

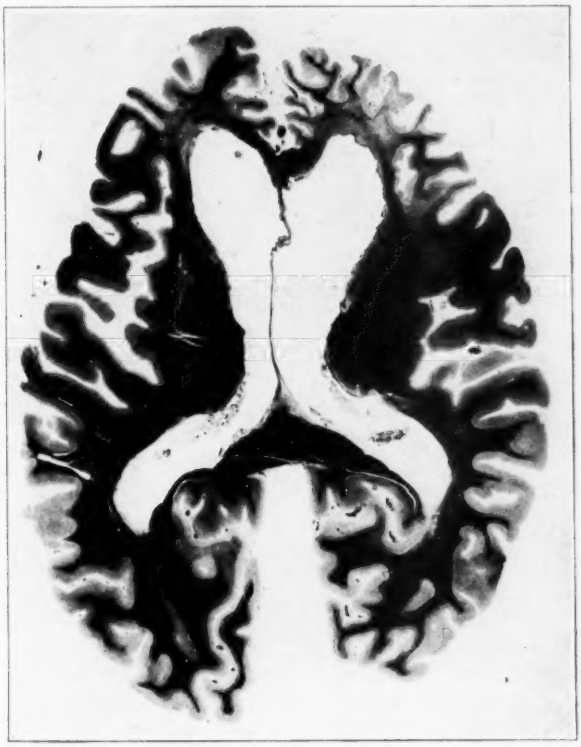

Fig. 11 (case 3).—Photograph of a horizontal section of the brain, showing severe atrophy of the corpus callosum (genu) and the frontal lobe, frontal part of the operculum and island on both sides. Hydrocephalus internus is evident.

Physical examination revealed nothing abnormal; all the normal reflexes were present, and no pathologic reflexes were found.

The spinal fluid contained a trace of globulin, but the colloidal gold and mastic reactions of the spinal fluid and the Wassermann reactions of the spinal fluid and blood were negative.

Course of Illness.—A brief record stated that the patient was greatly confused and disoriented during his entire stay in the hospital, making mental examination impossible.

A few months before death his physical condition began to decline, and death occurred on April 25, 1933. The known duration of the disease was approximately six years.

Gross Pathologic Observations.—The brain weighed 890 Gm. and was asymmetrical, the left side being smaller than the right. The convolutions of both hemispheres were distinctly atrophic. In the frontal lobes the atrophy involved the anterior and medial frontal gyri, approximately equally on the two sides. Broca's area was moderately atrophic. On the median surface the atrophy was about evenly distributed over the entire surface, without showing focal accentuation.

At the base of the frontal lobes the gyrus rectus and gyri orbitales were distinctly and uniformly atrophic.

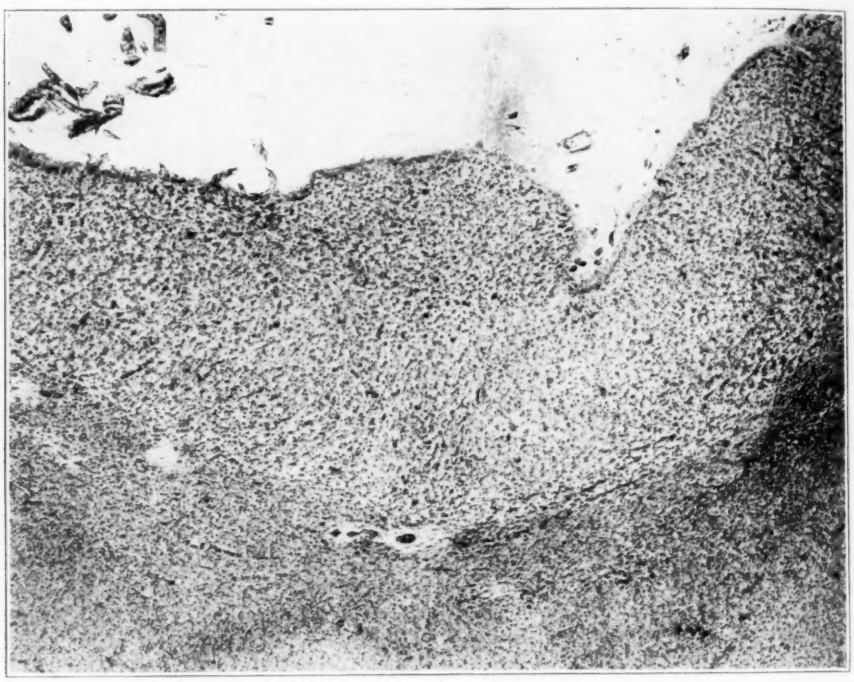

Fig. 12 (case 3).—Photomicrograph of a section of the cortex, showing severe damage of the architecture and status spongiosus. Van Gieson stain; Zeiss planar lens, 20 mm.

The atrophy overlapped the precentral sulcus and appeared to be accentuated in the anterior central gyrus and in the region of the gyrus angularis, distinctly more on the left than on the right.

In the occipital lobes there were foci of atrophy in the lateral occipital gyri. The temporal lobes were uniformly and moderately atrophic.

In frontal sections the gray matter was well outlined but very narrow. The white matter was reduced in width, and the lateral ventricles were enlarged.

The basal ganglia were half the normal size, both caudate bodies being severely atrophic. The capsula interna was much better preserved, appearing three times as wide as the nucleus caudatus.

The putamen, pallidum and thalamus were moderately reduced in size.

The hypothalamus, the red nuclei and the subthalamic bodies were indistinctly outlined. The substantia nigra was narrow and pale.

The pons, medulla and cerebellum were considerably reduced in size, weighing 95 Gm., but presented a normal appearance on cross-section.

The basal vessels were delicate.

Autopsy disclosed miliary tuberculosis.

Sections stained by the Weigert method revealed no demyelinization of the white matter of the hemispheres, but the myelin was greatly reduced in the striatum and pallidum. The myelo-architecture was severely damaged in the frontal and temporal lobes, the tangential fibers being almost entirely destroyed.

The pons, medulla and cerebellum presented normal outlines.

Histologic Observations.—The leptomeninges were moderately thickened, but otherwise there was no pathologic change.

The gray matter showed most severe changes, cyto-architectural disturbances dominating the picture. The entire cortex was involved. Three types of changes could be distinguished: (1) areas in which layers II and IV were greatly rarefied, the remaining layers being better preserved; (2) areas in which layers III, V and VI were more severely affected than layer IV, and (3) areas in which the entire cortex was greatly rarefied.

The atrophy was everywhere of purely degenerative type, inflammatory changes being absent. The blood vessel system appeared normal. The glial response was moderate. Astrocytes were frequently observed in the first layer, and there were microglial elements diffusely scattered throughout the cortex. The neurons showed nonspecific changes, chiefly of the so-called severe or chronic Nissl types. Inflated neurons were not present. Senile plaques, changes in the fibers of the Alzheimer type and argentophilic bodies were not observed.

Basal Ganglia: Caudate body and putamen: The parenchyma had undergone an extremely severe change. The smaller neurons had disappeared, but a few of the larger were observed. The glial response was active, and there was a dense network of glial fibers. There were countless round or oval glial elements containing fine greenish pigment in the cytoplasm. These cells resembled those encountered in Wilson's disease but were somewhat smaller. The pallidum was well preserved, but the glial response was active, and in places status spongiosus was present.

Thalamus: The neurons showed changes similar to those of the cortex, but they were not reduced in number. The glia response was mild. The numerous gray nuclei of the hypothalamus presented the same condition as those of the thalamus.

The substantia nigra was most severely affected, the parenchyma consisting of a few shrunken neurons containing little or no pigment. The production of glial fibers was marked.

The pons, medulla and cerebellum showed no pronounced changes except for considerable glial activity and shrinkage of the neurons in the olives.

COMMENT ON THE CLINICAL PICTURE

The ages of the patients vary from 30 (von Braunmühl [2]) to 75 years (Pick [1]), in the majority of cases the disease having developed between the middle of the fifth and the end of the seventh decade of

2. von Braunmühl, A., in von Bumke, O.: Handbuch des Geisteskrankheiten, Berlin, Julius Springer, 1931, vol. II, pt. 7, p. 673.

life. The duration of the disease varies from two and one-half to twelve years, the average duration being from four to six years.

Neurologic abnormalities were noted in some cases: stiff pupils (Liepmann [3]), unequal pupils (Lemke [4]), disturbance of gait or clumsy gait (case 1) and occasionally contractures (van Husen [5]). The superficial and deep reflexes are usually normal. Schmitz and Meyer [6] described the so-called *Atz* reflex, which consists of opening the mouth when any object is held in front of it (bread, burning match, etc.), and in the advanced stage grasping, swallowing, masticating, leaking and sucking reflexes.

Most authors have reported attacks which were described either as fainting or as epileptiform seizures. In the case described by Schmitz and Meyer [6] there were twitching of the face and limbs, grinding of the teeth, pallor and irregularity of the pulse. Frequent epileptiform seizures followed by mental clouding and confusion were reported by von Braunmühl and Leonhard.[7]

Focal Symptoms.—These may be subdivided into symptoms of involvement of (1) the frontal or (2) the temporal lobe. To the former group belong the peculiar changes of the nucleus of personality: lack of critique and initiative, ethical defects, lack of judgment and initiative muteness (Lemke [4]). Aphasia is attributed to atrophy of the temporal lobe.

Psychiatric Picture.—Schneider [8] distinguished three stages: (1) an early stage, which merges imperceptibly into (2) the stage of the fully developed clinical picture and (3) the final stage, with complete deterioration.

The first symptoms are usually noted by the family and consist of peculiar changes in personality. The patient becomes aimlessly overactive, roams for hours in the streets and is irritable, angry and difficult to manage. Professional interests and household duties are neglected. A frequent observation is moral deterioration and loss of the sense of propriety. Women occasionally become sexually promiscuous (Schneider [8]). Other patients steal, prevaricate, contract debts, collect trash and act thoughtlessly and carelessly. Disturbances of memory are common. School knowledge and memory for past events are retained for a long time, but memory for recent events is severely impaired (cases 2 and 3). Stertz [9] found only mild defects of memory in his case. Perception is retained for a long time in some instances.

Disturbance in speech is one of the most important symptoms and consists either of diminution of voluntary speech (sensory or motor aphasia) or pressure of speech. These disturbances may occur at a very early stage and progress rapidly, reducing the spoken language

3. Liepmann: Neurol. Centralbl. **19**:328, 1900.

4. Lemke, R.: Arch. f. Psychiat. **101**:623, 1934.

5. van Husen, T.: Allg. Ztschr. f Psychiat. **101**: 381, 1934.

6. Schmitz, H. A., and Meyer, A.: Arch f. Psychiat. **99**: 747, 1933.

7. von Braunmühl, A., and Leonhard, K.: Ztschr. f. d. ges. Neurol. u. Psychiat. **150**: 209, 1934.

8. Schneider, C.: Monatschr. f. Psychiat. u. Neurol. **65**: 230, 1927.

9. Stertz, G.: Ztschr. f. d. ges. Neurol. u. Psychiat. **101**: 729, 1926.

to a few fragmentary words, so that the patient appears almost mute. He murmurs the same few words or meaningless sentences over and over (cases 1 and 3). Occasionally words are distorted. Schmitz and Meyer [6] stated that mute patients could still be stimulated to sing.

Stertz [9] described a patient who manifested pressure of speech, answering questions with an irrelevant flood of words accompanied by lively mimicry. Some patients (cases 2 and 3 and Rosenfeld [10] and Heilbronner [11]) manifested no definite disturbances in speech.

The duration of the first stage is difficult to determine, since it varies considerably. It merges imperceptibly into the second, which is characterized by increasing deterioration. Orientation may be wholly or partially preserved; spontaneous speech may show no gross defects, and memory for past events is usually retained. A certain insight may be preserved. The patient's social behavior may be correct, and he is able to carry on simple duties; yet examination discloses an advanced stage of deterioration (Rosenfeld [10]).

The last stage is characterized by complete deterioration, definite physical decline and rapid loss of weight, not associated with pathologic changes in the internal organs.

Death occurs from the physical decline or from intercurrent disease.

GROSS PATHOLOGIC APPEARANCES

According to von Braunmühl [2] the gross pathologic changes can be divided into atrophy of three types: (1) frontal, (2) temporal and (3) parietal. This subdivision is somewhat schematic, since combined types (frontotemporal or frontotemporoparietal) are frequent. Atrophy of more than three lobes (frontotemporoparieto-occipital, Altmann [12]) possibly represents an incomplete generalized type. Therefore, it appears justifiable to distinguish in addition to the preceding three types (4) a combined and (5) a generalized type.

Atrophy of the frontotemporal type is most frequent. Usually it terminates abruptly in the region of the sulcus precentralis. The insula is usually involved, frequently showing more severe damage in the anterior part. One hemisphere, the left in the majority of cases, is more atrophic (von Braunmühl [2]). The base of the frontal lobe is regularly involved, but the atrophy varies in severity. The atrophy of the median surface is usually limited to the anterior parts of the superior frontal gyrus and the gyrus cinguli and the anterior part of the corpus callosum. The atrophy of the temporal lobe involves either part or the entire lobe (cases 1, 2 and 3). Atrophy of the parietal and occipital lobes is less frequent (Pick,[1] Altmann,[12] Verhaart [13] and von Braunmühl [2]). In the parietal lobe atrophy is usually limited to the gyrus supramarginalis and gyrus angularis. Atrophy of the pons and cerebellum has rarely been reported (Verhaart,[13] case 1).

10. Rosenfeld, M.: Ztschr. f. Psychol. u. Neurol. **14**:115, 1909.

11. Heilbronner: Arch. f Psychiat. **33**:366, 1900.

12. Altmann, E.: Ztschr. f. d. ges. Neurol. u. Psychiat. **83**:610, 1923.

13. Verhaart, W. T. G.: Nederl. tijdschr. v. geneesk. **74**:5586, 1930.

HISTOLOGIC PICTURE

The histopathologic structure of Pick's disease is characterized by equally severe involvement of all parts of the nerve tissue: parenchyma, axis-cylinders, myelin sheaths and glial structures.

The cyto-architectural disturbances are usually, but not always, of the layer type, layers II and III a being most commonly affected and layers III b and IV less frequently damaged (von Braunmühl,[2] Altmann,[12] Schneider [8] and others). Altmann [12] noted severe destruction of the lower layers in areas with particularly pronounced destruction of myelin. The selective degeneration of certain layers led some authors to assume a systemic involvement of the layers of the cortex (Altmann,[12] Jacob,[14] Onari and Spatz [15] and von Braunmühl [2]). Altmann [12] interpreted the histologic picture as a pathoclisis of the third and fifth layers. Von Braunmühl and Leonhard [7] attempted to determine the lobes primarily affected. Jacob [14] emphasized the importance of destruction of myelin and assumed that the degeneration of the cortex was secondary. While this view warrants consideration, a critical review of my cases and of the literature suggests simultaneous affection of the gray and the white matter.

The degeneration of the neurons can be subdivided into two groups: nonspecific and specific.

The first group is characterized by simple shrinkage or swelling of the neuron, disappearance of the intracellular structure and accumulation of granules in the nucleus. The specific changes have been described by Alzheimer [16] and are visible in sections impregnated with silver and in Nissl preparations. The neurons become inflated, and the perinuclear plasma appears homogeneous and stains a deep blue or pinkish gray. In sections impregnated with silver intracellular argentophilic bodies can be demonstrated frequently, varying in size from small granules to a huge mass filling the cytoplasm and displacing the nucleus. They stain deep black.

The glia displays considerable activity, producing abundant fibers, which is frequently encountered in chronic degenerative conditions. Products of disintegration are usually limited to scattered lipoid droplets in the glial elements and perivascular spaces. The spongy state is a common but not a constant occurrence. It is restricted to the upper layers (layers II and III).

The blood vessels show no changes in the majority of cases. Senile plaques and changes in the fibers of the Alzheimer type are usually absent; there were none in the cases described in this paper. Scattered plaques have occasionally been reported.

Pathologic changes in the basal ganglia are not constant. Definite changes have been described only in cases of gross atrophy of the striate bodies. Detailed description has been given by von Braunmühl,[2] who reported reduction in the numbers of neurons, inflated elements and protoplasmic and fibrous glia cells and the spongy state.

Involvement of the cerebellum has been mentioned by Verhaart,[13] but no detailed description was given. In case 1 such an involvement

14. Jacob, A., cited by von Braunmühl.[2]

15. Onari, K., and Spatz, N.: Ztschr. f. d. ges. Neurol. u. Psychiat. **101**:470, 1926.

16. Alzheimer, A.: Ztschr. f. d. ges. Neurol. u. Psychiat. **4**:356, 1911.

was shown. The histologic changes were identical with those in the cerebral hemispheres, consisting of degeneration of parenchyma and demyelinization.

The histologic changes of degenerated myelin sheaths are nonspecific, the sheaths appearing narrow, fragmented and tortuous. The demyelinization is not complete, moderate amounts of myelin being retained in the atrophic areas.

The axis-cylinders are frequently reduced to a few scattered fragments.

PATHOGENESIS

Pick [17] considered the disease to be a type of senile dementia with focal lesions and distinguished it from ordinary diffuse senile atrophy. The original view of Pick [17] is no longer tenable. Few patients belong in the senile age group, the majority hardly reaching the presenile years. It must be assumed, therefore, that Pick's disease may occur at widely differing periods of life.

Gans [18] observed a close conformity of the atrophic areas with the cyto-architectural fields of Brodmann and expressed the belief that the atrophy involves principally phylogenetically younger parts of the brain, i. e., the areas which are absent or rudimentary in animals. This view has not been confirmed. Onari and Spatz [15] observed no conformity between the cyto-architectural fields and the areas of atrophy. Subsequent studies have demonstrated that the changes involve much larger areas of the brain than was assumed by early investigators, and recent observations show that, in reality, the entire brain is affected.

Genealogic studies suggest that in some instances there is a hereditary trend in Pick's disease. It has been observed in several generations, in siblings and in association with other hereditary nervous disorders. Grünthal [19] reported five instances of Pick's disease in two generations, the symptoms occurring between the ages of 42 and 45. Von Braunmühl and Leonhard [7] observed the disease in two siblings. Schmitz and Meyer [6] reported cases of Pick's disease in two generations. In the first generation the disease was suspected in two brothers; a daughter of one brother had Pick's disease; the son of the second possibly also had the same disorder, and a grandson was feebleminded. In Verhaart's [13] observation there was a possible association of Pick's disease with Marie's atrophy in two sisters of a family with outspoken hereditary taint, while von Braunmühl [20] reported a case in which Pick's disease was combined with amyotrophic lateral sclerosis. Korbsch [21] found a case in which there was possible association of Pick's disease with Huntington's chorea. Hascovec [22] described a patient aged 60 whose father was alcoholic and had senile psychosis; the mother had paralysis agitans; two sisters probably had Pick's disease, and the patient's son was feebleminded.

17. Pick, A.: Monatschr. f. Psychiat. u. Neurol. **16**:378, 1904.
18. Gans, A.: Ztschr f. d. ges. Neurol. u. Psychiat. **80**:10, 1922.
19. Grünthal, E.: Ztschr. f. d. ges. Neurol. u. Psychiat. **136**:464, 1931.
20. von Braunmühl, A.: Zentralbl. f. d. ges. Neurol. u. Psychiat. **48**:358, 1931.
21. Korbsch, H.: Arch. f. Psychiat. **100**:326, 1933.
22. Hascovec, V.: Zentralbl. f. d. ges. Neurol. u. Psychiat. **73**:345, 1934.

PSYCHIATRIC, NEUROLOGIC AND NEUROPATHOLOGIC STUDIES IN DISSEMINATED ALTERATIVE ARTERIOLITIS

LAURETTA BENDER, M.D.
NEW YORK

Disseminated alterative arteriolitis is a disease entity which may be best understood by an analysis of the literature which led to the concept of acute bacterial endocarditis and what is known in the United States as Libman-Sacks' disease, or verrucous endocarditis without bacteremia. The two cases to be discussed are of interest because of the cerebral symptomatology and the presence of the typical vascular lesions in the brain as well as in other organs of the body, although endocarditis was not present in either case.

In acute bacterial endocarditis the endothelial lining of the heart responds with proliferative changes on the wall and especially on the valves; verrucous masses are formed by the acquisition of thrombotic material consisting of fibrin, blood platelets and leukocytes of the blood stream, and the underlying inflammatory processes are secondary. In the subacute process of Libman-Sacks' disease bacteremia cannot be proved, and the inflammatory reaction is less marked, but verrucous growths occur by endothelial proliferation and thrombotic processes on the valves and walls of the heart. Similar processes occur in other parts of the vascular bed, due also to proliferation of the endothelial lining of the vessels and thrombotic processes. In other subacute septicemic conditions it is possible for the endocardium to remain free from any pathologic change, while the endothelial lining of the smaller ramifications of the vascular system, namely, the arterioles and capillaries of the internal organs, may show alterative and proliferative changes.

Libman [1] first classified the types of endocarditis as syphilitic, rheumatic, acute and subacute bacterial and indeterminate, and in so doing he first recognized the nonrheumatic, nonbacterial form of verrucous endocarditis under the term indeterminate. In indeterminate verrucous endocarditis there are no Aschoff bodies in the myocardium. In general, the microscopic lesions of the myocardium are specific for the different types of endocarditis. In acute bacterial endocarditis any demonstrable

Read at the International Neurological Congress in London, Aug. 1, 1935.

From the Psychiatric Division and the Department of Pathology of the Bellevue Hospital and the New York University College of Medicine.

1. Libman, E.: The Characterization of the Various Forms of Endocarditis, J. A. M. A. **80**:813 (March 24) 1923.

lesion consists of polymorphonuclear leukocytes; in subacute bacterial endocarditis there may be observed round cell interstitial lesions, or the so-called Bracht-Wächter bodies; in rheumatic endocarditis Aschoff bodies are to be noted, and in syphilitic endocarditis the usual syphilitic lesion may be present in the myocardium. In these disease entities, according to Libman, the renal pathologic picture is always significant; renal infarcts and embolic phenomena may occur in all types; other forms of renal disturbance are not common in association with bacterial or rheumatic endocarditis, except in the bacteria-free stage of subacute bacterial endocarditis, in which the glomeruli show reactive changes. Libman and Sacks [2] more fully elaborated the clinical and pathologic picture of what they called atypical verrucous endocarditis, which has become known as Libman-Sacks' disease. Emphasis was placed on the verrucous nature of the endocardial lesion, the sterile blood culture, the absence of Aschoff or Bracht-Wächter bodies in the myocardium, the acute glomerular nephritis, the petechiae and other lesions in the skin, the progressive anemia and the subacute course. Baehr [3] studied the problem of glomerular nephritis and showed that it was rare in rheumatic fever as compared with subacute streptococcic endocarditis and was much more common in the bacteria-free stage of the latter disease. However, he claimed that in the nonbacterial verrucous endocarditis of Libman glomerular nephritis is commonly associated with a diffuse vascular disease which affects the endothelium of the capillaries, arterioles and venules not only of the heart and kidney but of the entire body. Baehr's [4] first description of these vascular lesions was based on a study of seventeen cases and is classic and complete.

> Some toxic agent, probably of bacterial origin, primarily damages the endothelium of capillaries (in the kidneys, skin and other organs), arterioles, small arteries, small veins and venous capillaries. . . . The endothelium . . . especially of the capillaries and arterioles, becomes swollen, proliferates actively and undergoes necrosis. The lumen of the affected vessels then becomes partially or completely occluded by a mixture of proliferated and disintegrating endothelial cells and thrombotic material. Sometimes the proliferative lesion within the lumen may give the appearance of an intimal granuloma. . . .
>
> In places where an arteriole or small artery has been denuded of its endothelium and the lumen partially or completely occluded the wall may appear as if infiltrated with serous effusion or may even show evidences of arterial necrosis. Where the

2. Libman, E., and Sacks, B.: A Hitherto Undescribed Form of Valvular and Mural Endocarditis, Arch. Int. Med. **33**:701 (June) 1924.

3. Baehr, G.: Glomerular Nephritis in Rheumatic Fever and Its Significance, in Contributions to the Medical Sciences in Honor of Dr. Emanuel Libman by His Pupils, Friends and Colleagues, New York, International Press, 1932, vol. 1, p. 125.

4. Baehr, G.: Renal Complications of Endocarditis, Tr. A. Am. Physicians **46**:87, 1931.

vascular damage is old the lumen may be found to be occluded by granulation tissue in which recanalization is sometimes evident.

No mention was made of specific studies of the vessels of the brain. Gross [5] made a more intensive study of the pathologic changes in the heart in this disease and described the vascular lesions in the heart as "granular plugged vessels"; he claimed that the granular plugs stain especially well with Mallory's phosphotungstic acid hematoxylin. He compared the granular plugs to the verrucous growths on the valves. He claimed that there is a proliferation of the valvular, mural or vascular endothelium, accompanied by swelling and granular and hyaline changes of the endothelial cells, and that, while the hyaline substance stains red, the granules stain blue because they arise from the karyorrhectic nuclei of the necrotic cells. In summarizing, he stated: "It appears that this type of lesion may arise logically in the affected vessels. It seems possible, however, that many of these 'granular plugged vessels' may also be due to embolization from the broken-off fragments of the valvular lesions." This, however, would make the two lesions of the same origin.

Fahr [6] approached the subject from the point of view of the kidney and developed a concept of malignant nephrosclerosis in which, he stated, the renal lesion is secondary to inflammatory processes in the blood vessels, which he designated as necrotizing arteriolitis or productive endarteritis. He referred the damage to rheumatism, syphilis and lead. Klemperer and Otani [7] described sixteen cases and emphasized the vascular changes, which they called arteriolonecrosis and which they stated are primary to the glomerular changes. They ascribed the vascular lesions possibly to the effect of various toxins on vessels that have already suffered simple degenerative atherosclerosis (in connection with antecedent hypertension).

Somewhat comparable vascular lesions have also been described in other conditions. Strang and Semsroth [8] described a case in which vascular lesions were associated with streptococcic septicemia. His case, which was closely similar to one of the cases reported in this paper, was that of a young man who suffered from low grade streptococcic septicemia, with a subacute clinical course and a maximum temperature of 100.4 F. The cardiac findings suggested rheumatic endocarditis; blood cultures contained Streptococcus viridans, and the termination

5. Gross, L.: The Heart in Atypical Verrucous Endocarditis, in Contributions to the Medical Sciences in Honor of Dr. Emanuel Libman by His Pupils, Friends and Colleagues, New York, International Press, 1932, vol. 2, p. 527.

6. Fahr, E.: Virchows Arch. f. path. Anat. **226**:119, 1919.

7. Klemperer, P., and Otani, S.: Malignant Nephrosclerosis (Fahr), Arch. Path. **11**:60 (Jan.) 1931.

8. Strang, J. M., and Semsroth, K.: Streptococcic Septicemia with Vascular Lesions, Arch. Int. Med. **47**:583 (April) 1931.

was with uremia. Grossly the heart showed slight excrescences on the mitral valve, with hemorrhagic infiltration. Histologic studies showed alterative, productive and obliterative arteriolitis of the heart and kidneys. The clinical course seemed to depend on the relative magnitude of involvement of the vessels of the various organs. The authors advanced this view:

> This case, on the basis of the anatomic and clinical evidence, was fundamentally one of low grade sepsis in which the principal tissue reaction of the host is this unusual vascular lesion. The low virulence of the organism may be assumed to have permitted the development of the process for a prolonged period without the production of the typical host-tissue reaction to infection. The inevitable but latent symptomatology was therefore referred to the vital organs which failed secondarily to their local circulatory impairment. Such a process might be contrasted with "subacute bacterial endocarditis," which is also due to a streptococcic invasion, but with typical septic manifestations. In this disease the brevity of the course might preclude the development of the characteristic vascular lesions that were found in this case.

The cerebral changes were not described in this case. However, Siegmund,[9] in a brief article, mentioned the occurrence of alterative arteriolar changes, with necrosis of the walls of the vessels of the brain as well as of the kidney, in cases of chronic streptococcic sepsis.

Endarteritic changes in the brain were first studied in 1904 by Nissl[10] and Alzheimer[11] in cases of syphilitic endarteritis; they noted swelling and proliferation of the cells of the intima, sometimes with narrowing of the lumen and obliteration of the vessels of the pia and cerebral cortex. Similar observations in syphilitic processes have since been made by Jacob[12] and Spielmeyer.[13] It has been claimed that, unlike other syphilitic conditions of the brain, these endarteritic processes are probably of toxic origin, since spirochetes have not been observed in the brain in such cases and inflammatory responses were absent. It is of considerable interest that these observations and the conclusions derived from them are similar to those already made in relation to the endarteritic processes in the internal organs in response to subacute streptococcic infection. The less active the process the less likelihood there is of finding the organism or of observing an inflammatory response in the tissues and the greater the endothelial

9. Siegmund, W.: Centralbl. f. allg. Path. u. path. Anat. **35**:276, 1924.

10. Nissl, F.: Zur Histopathologie des paralytischen Rindenerkrankungen, in Nissl, F., and Alzheimer, A.: Histologie und Histopathologie: Arbeiten über die Grosshirnrinde, Jena, Gustav Fischer, 1904, vol. 1.

11. Alzheimer, A.: Progressive Paralyse und endarteritische Hirnlues, Centralbl. f. Nervenh. **16**:443, 1905.

12. Jacob, A.: Ueber die Endarteritis syphilitica der Kleinhirnrindengefässe, Ztschr. f. d. ges. Neurol. u. Psychiat. **54**:29, 1920.

13. Spielmeyer, W.: Histopathologie des Nervensystems, Berlin, Julius Springer, 1922, vol. 1, p. 223.

response in the smaller vessels. There has been a tendency to refer to the more active process, in which also the organism may be isolated, as "inflammatory" and to the less active process with the typical endothelial reaction as "toxic." The difference is probably quantitative and not qualitative.

Winkelman and Eckel [14] reported two cases of productive endarteritis of the smaller vessels of the cortex in association with toxemia due to food poisoning. The process is described as diffuse, involving the smaller vessels of all parts of the brain and also the pial vessels and the pia. In some places small areas of secondary softening were associated with the vascular lesions. Winkelman and Eckel expressed the belief that the endothelial proliferation was in response to the toxemia and that it was comparable to lesions described in the literature in cases of severe intoxication with lead, manganese, carbon monoxide and arsenic and to experimental lesions produced in animals with metallic poisoning, as well as to the lesions observed in cases of the syphilitic endarteritic processes which have been mentioned. Winkelman and Eckel [15] also studied the cortical changes in five cases of acute rheumatic fever with neurologic and psychiatric symptoms. They noted changes which they claimed were not specific for the disease studied but were such as might be expected in any case of acute toxemia or infection. They claimed that the cerebral edema was more important than the hyperpyrexia. Endarteritis of the smaller vessels with endothelial swelling was observed in every case, and they expressed the belief that it was due to the mechanical factor of edema in the perivascular spaces as well as to the irritative factor of the toxin in the blood stream. The endarteritis, although diffuse, was not uniform in its distribution but occurred in patches. This, in their opinion, accounted for the variations in the clinical picture and also explained the *Verödung*, or acellular areas. Embolic phenomena occurred in connection with the endarteritis, and petechial hemorrhages resembling those seen in purpura were also present in the brain and were usually associated with similar lesions in the skin. Winkelman and Eckel [16] in a similar way described seven other cases of cerebral endarteritis in association with various forms of severe infection and toxemia. They discussed the probability that the proliferation of the endothelial lining is an expression of the acute toxic stage and that if the patient recovers from

14. Winkelman, N. W., and Eckel, J. L.: Productive Endarteritis of the Smaller Cortical Vessels in Severe Toxemia, Brain **50**:608, 1927.

15. Winkelman, N. W., and Eckel, J. L.: The Brain in Acute Rheumatic Fever: Nonsuppurative Meningo-Encephalitis Rheumatica, Arch. Neurol. & Psychiat. **28**:844 (Oct.) 1932.

16. Winkelman, N. W., and Eckel, J. L.: Endarteritis of the Small Cortical Vessels in Severe Infections and Toxemias, Arch. Neurol. & Psychiat. **21**:863 (April) 1929.

the toxemia the endarteritic changes may also regress and disappear. Associated with cerebral endarteritis in the acute stages are secondary changes, such as paling and swelling of the ganglion cells due to the cutting off of the blood supply as well as to the direct action of the toxin, and this process is also reversible in case of recovery. In this discussion it is pointed out that the smaller vessels of the gray substance are involved more severely than those in the white tracts. This is explained on the basis of the structure of the vascular bed, in accordance with the work of Pfeifer,[17] who claimed that the vessels to the gray matter arise in the meninges, enter the gray matter a short distance and branch immediately to correspond with the architecture of the cortex, while those going to the white tracts pass through the gray matter and follow the tracts of the subcortical white area. These last-mentioned vessels are said to be involved in Schilder's periaxial encephalitis and in Binswanger's subcortical encephalomalacia.

Zimmerman and Yannet [18] reported the case of an infant with pneumococcic septicemia associated with lobar pneumonia. The child had been spastic on the right side and had had convulsions. Blood culture revealed Pneumococcus type IV, and the spinal fluid was clear. The brain showed that "the smaller blood vessels of the cortex and central grey regions had swollen endothelium and their walls had a peculiar hyalin translucency." Besides this there was degeneration of the nerve cells of the same regions, and there appeared to be a positive association between the two disturbances. There was no inflammatory reaction of any kind. There were associated destruction of myelin and phagocytosis of fat in the same regions and active protoplasmic glial proliferation in the area of destruction of the ganglion cells. The authors pointed out that this is not the typical suppurative encephalitis which might be expected with pneumococcic septicemia but claimed that the vascular changes suggested toxic encephalitis instead. They recognized that the same virus or toxin may induce either the direct inflammatory or the so-called toxic reaction and that the other cerebral changes may be due either to the direct effects of such virus or toxins or to the anoxemia dependent on the reduction of the blood supply through the endothelial thickening and possible vascular occlusions, either functional or organic. It is of importance that the same distribution is shown as in the cases reported by Winkelman and Eckel, namely, in the cortex and central gray matter. De Vries [19] reported four cases of acute disease of the

17. Pfeifer, R. A.: Die Angioarchitektonik das Grosshirnrinde, Berlin, Julius Springer, 1928, vol. 3.

18. Zimmerman, H. M., and Yannet, H.: Cerebral Changes in Pneumococcus Septicemia, J. Nerv. & Ment. Dis. **75**:386, 1932.

19. de Vries, E.: Acute Diseases of the Brain Due to Functional Disturbance of the Circulation: Laminated Cortical Disease, Arch. Neurol. & Psychiat. **25**:227 (Feb.) 1931.

brain due to functional disturbances of the circulation. In two cases these were associated with eclampsia, uremia and a sudden fall in blood pressure, and in two others, with shock and sunstroke. In these cases there was elective softening of the cortex, without vascular changes. In all but one case the softening took the form of laminated necrosis involving from the third to the fifth layer of Brodmann. De Vries expressed the belief that the lesions were due to functional disturbances in the circulation, which produced ischemic changes. He asserted that the initial disturbance was in the endothelial cells of the vascular wall and was due either to spasm of the vessel or to lowering of the blood pressure through systemic disease. The distribution of the lesion is therefore dependent on the architectonics of the vascular bed. In this he took issue with the Vogts,[20] who had advanced their theory of pathoclisis based on the argument that the tendency to cortical lesions in the third cortical layer is due to an elective vulnerability of the affected part, without any influence from the vascular distribution. Hiller [21] called attention to the vascular distribution as the basis for the electivity of lesions of the central nervous system, and this principle has been further emphasized by Bender and Schilder and Bender [22] in connection with alcoholic encephalopathy.

Pfeifer [17] and Cobb and Cobb and Blain [23] have given the fullest description of the angio-architectonics. A review of the subject is important for an understanding of the material to be presented in this paper. Cobb and his associates showed that the blood supply of the cerebrum is furnished by three branches from the circle of Willis, which pass over the surface of the hemispheres with the meninges and send perforating arteries to the cortex through the pia. The gray matter is more richly supplied than the white. As the smaller arteries plunge into the cortex, small arterioles and capillaries are given off at right angles. These are most numerous in the third, fourth and fifth cortical layers. Throughout the central nervous system the gray matter is more

20. Vogt, C., and Vogt, O.: Erkrankungen der Grosshirnrinde im Lichte der Topistik, Pathoklise und Pathoarchitektonik, Jahrb. f. Psychiat. u. Neurol. **28**:1, 1922.

21. Hiller, F.: The Electivity of Diseases of the Nervous System, Arch. Neurol. & Psychiat. **20**:145 (July) 1928.

22. (*a*) Bender, L., and Schilder, P.: Encephalopathia Alcoholica (Polioencephalitis Haemorrhagica Superior of Wernicke), Arch. Neurol. & Psychiat. **29**:990 (May) 1933. (*b*) Bender, L.: Myelopathia Alcoholica Associated with Encephalopathia Alcoholica, ibid. **31**:310 (Feb.) 1934.

23. Cobb, S., and Blain, D.: Arteriosclerosis of the Brain and Spinal Cord, in Cowdry, E. V.: Arteriosclerosis: A Survey of the Problem, New York, The Macmillan Company, 1933, chap. 14, p. 397. Cobb, S.: The Cerebral Spinal Blood Vessels, in Penfield, W.: Cytology and Cellular Pathology of the Nervous System, New York, Paul B. Hoeber, Inc., vol. 2, chap. 12, p. 577.

abundantly supplied with arterioles and capillaries than the white matter. Wherever a nucleus lies amid white tracts, the contrast between the vascular supply to the gray matter and that to the white substance is conspicuous. There are a fine, round meshwork forming a rich capillary bed in the nucleus and an open, angular mesh in the white spaces, where the capillaries tend to run parallel to the tracts. Vessels enter a ganglion from all directions and plunge toward the center, branching freely into a fine network. The blood supply to the cerebellum needs special description. The pial surface of the cerebellum is rich in vessels, from which small arteries plunge into the molecular layer and pass through it, giving off a few capillaries toward the granular layer. Between the molecular and the granular layer many capillary loops are given off about the Purkinje cells and from there pass into the molecular layer.

REPORT OF CASES

Two cases are reported, in one of which disseminated alterative arteriolitis developed in a young man in connection with an obscure infection, which probably started in the upper respiratory tract or the lungs. In the second case somewhat less typical arteriolitis developed in a young Negress in connection with postabortal sepsis.

CASE 1.—*History.*—E. B., a white man aged 27, born in the United States, single, a clerk, was brought to the psychiatric pavilion of the Bellevue Hospital on Dec. 24, 1933. According to the history given by a sister, he had been well until five weeks before, when the illness started with headache and lassitude; the headache progressed during the ensuing week; he became nauseated and vomited and began to "talk out of his head"; he was taken to a local hospital. A report from this hospital stated: "The patient was admitted on November 27 and discharged on December 2. The diagnosis was bronchopneumonia (postinfluenzal), with secondary toxic encephalitis. For about ten days the patient had complained of lassitude and a dull headache, which became more severe and was accompanied by nausea and vomiting. On December 2 he had recovered from the bronchopneumonia. Neurologic examination revealed nothing abnormal, except psychomotor retardation. Roentgenographic examination of the chest on November 28 showed deficient aeration of the right lung and a few scattered areas of infiltration in the lower lobe which suggested bronchopneumonia; the left lung was clear. He was discharged as much improved."

The sister said that a lumbar puncture yielded normal fluid. Although he seemed improved when he was discharged from the hospital, he had headache and vomited when he arrived home; he seemed a little better after a week. A few days before his admission to the Bellevue Hospital he began to "see things"; he spoke of bugs, telephones, boats and the like. The night before his admission he told a friend that he had a wonderful pair of double glasses, from which it was inferred that he had diplopia.

Examination.—On his admission the patient seemed confused, bewildered, partially disoriented and had hallucinations, but he comprehended and cooperated well. He said: "I came sick all of a sudden with stomach trouble. It came all of a sudden. It came on, and I took sick. I've been vomiting. I had headaches. I

was at the hospital for awhile—about four weeks ago. Today is the 20th of December 1934. I've seen accidents. I saw one there." (According to the sister the patient actually had had an automobile accident about three months before.) "A sort of collapse. The body stopped breathing. I thought it was my own body. There were other things up there. I heard voices saying 'we ought to do this or that.' I don't remember seeing anything double. I feel weak generally."

There were hemorrhages in both ocular fundi; the veins in the left eye were markedly engorged; the disks did not show blurring or elevation. There were a few nystagmoid jerks on looking to the left. The pupils were equal and regular and reacted normally to light and in accommodation. The fifth, seventh and ninth cranial nerves were intact. The voice was thick. The gait was slightly titubating. The Romberg test gave normal results. The patient stood poorly on the left foot, and power in the left hand was diminished. The finger to nose test showed dysmetria with the eyes closed. The tendon reflexes were present and equal on the two sides. There were no sensory disturbances. The pulse was normal, and the patient was pale and undernourished.

Course of Illness.—On December 26 the patient said: "I can't make head nor tail of it. Right now I feel fine. It started with headaches about a week before Thanksgiving. They lasted about an hour. Some days I got them three or four times in the day. They were first in the forehead, like back of the eyes. One or two days I had a little temperature, like 100 or 102. I was sleeping a good deal of the time. I felt drowsy. Then I stopped getting the headaches. I was in the hospital at that time and stayed about a week. I stayed home afterwards. I had a funny feeling. I don't know how to explain it. Everything seemed to take longer. A couple of hours would seem like eight or nine hours. Then my legs would go to sleep every once in a while. I would get this numb feeling. I could move them, but it would be hard. It was an awful feeling. Then my arms would go to sleep, too. I saw a lot of bugs crawling around on the wall in the room. I saw a lot of pictures, too, like little dolls. They all said it was imagination at home, but I said it was real. 'It is your condition,' they would say." (Did you say your body stopped breathing?) "I did say something like that, but I can't remember now." (Date?) "Today is the 26th of December 1934." (Isn't it 1933?). "Jesus, you got me all mixed up now." (Do you feel like yourself?) "Sometimes, then again I feel like there is another organism put in me, like another part put in me. Once or twice I felt like I was somebody else. I didn't know who I was. I don't feel sick at all. I didn't want to come here. It was my mother's idea."

At this time he was in good contact but somewhat inappropriately euphoric. He showed lapses in attention, when he tended to mutter. There were retardation in the thought processes and difficulties in calculation. The next day he said: "I was seeing things the other day. I saw little bugs in the house. Maybe there were bugs in the house, but everybody else said there were not. I saw writing on the wall. That is about all I saw. It was not exactly sensible writing. You could read words, but there was nothing much there really to make sense. Sometimes time passes slowly; fifteen minutes seems like an hour. Sometimes the night went very slowly, too." The next day, December 28, he said: "I am here about eight days. This is the second Monday in January; I didn't celebrate New Year's yet. The first of January is New Year's. I don't think we have had New Year's yet. I think I am here about two weeks. I remember we celebrated Christmas here."

During this time the neurologic status was as follows: There was a tendency to sway to the left; the left arm had a tendency to deviate and sink, and the

fingers of the left hand tended to flex when the two arms were outstretched. Speech was slurred. The head was not sensitive nor the neck stiff. The pupils were round and equal and reacted to light. There was no nystagmus. The corneal and conjunctival reflexes were present. The fundi showed a patch of chorioretinitis in the right eye and small hemorrhages over both papillae, with blurring. The tendon reflexes of the arms were normal. The knee jerks were reduced, and the ankle jerks were absent. There were some ataxia in the finger to nose and ankle to knee tests and adiadokokinesis on the left. The visual fields were intact. There was reduced sensibility to pain over the entire body.

On his admission the patient was undernourished and pale. The ears, nose and throat were normal; the lungs were clear; the heart was normal; the pulse rate was 88 a minute; the temperature was 99.4 F., rectally, and the blood pressure was 130 systolic and 75 diastolic. The urine had a specific gravity of 1.019 and contained no albumin, sugar or acetone. The Wassermann reaction of the blood was negative. Spinal puncture was performed on December 29; the fluid was under normal pressure and was clear; it contained no cells or globulin; the Wassermann reaction and the colloidal gold curve were normal. A roentgenogram of the skull revealed nothing abnormal. Examination of the blood revealed 11,500 leukocytes, 83 per cent of which were polymorphonuclears, and 2,480,000 erythrocytes, with 60 per cent hemoglobin.

On January 3 there was a sudden change in the picture. The patient became stuporous and almost comatose, with labored breathing of the Cheyne-Stokes type. The rectal temperature was 99.8 F.; the pulse rate was 130 and the blood pressure 162 systolic and 90 diastolic. The internal organs, including the heart and lungs, were normal. The pupils were active. The right arm and leg were spastic, with pseudo-athetoid movements of the right hand, a Babinski sign and clonus, while the left side of the body was flaccid. By evening horizontal nystagmus and deviation of the head to the left had developed, and the Babinski sign was present on the right side. The spinal fluid was not under increased pressure; it was clear and contained no globulin and only 4 lymphocytes. The nonprotein nitrogen content of the blood was 38 mg. per hundred cubic centimeters and the sugar content 139 mg. The leukocytic count had risen to 21,700, with 93 per cent polymorphonuclear cells and evidence of the formation of new cells of this series; the erythrocyte count had dropped to 1,900,000. The temperature rose to 101 F.; the stupor increased, and the patient was incontinent and unable to swallow and perspired profusely. He died on January 4, at 8:30 p. m. A diagnosis of toxic encephalitis of unknown origin was suggested.

Gross Postmortem Examination.—This was performed the next morning.[24] The body appeared well developed and nourished. It measured 5 feet and 10 inches (177.8 cm.) and weighed 150 pounds (68 Kg.). A slight icteric tinge was present in the scleras. There were no other significant external manifestations. The serous sacs were free from adhesions or fluid. The lungs showed a few dark raised areas in the right lower lobe. The heart weighed 400 Gm.; the increase in weight appeared to be due to slight hypertrophy of the left ventricle. The

24. The postmortem examination and microscopic study of the body tissues were made by the department of pathology of the Bellevue Hospital under the direction of Dr. I. Graef. Dr. Graef described the lesions in the arterioles of the organs in somewhat different terms than I have used in describing similar lesions in the brain. He spoke of "hyaline and fibrinoid thrombotic masses . . . capped by proliferative endothelial cells," while I prefer not to refer to these masses as thrombotic, since they lie beneath or within the endothelial layer.

coronary vessels and the aorta were not abnormal. The spleen weighed 230 Gm., being slightly enlarged, soft and friable on section. The gastro-intestinal tract showed marked dilatation of the colon and a few petechial hemorrhages in the mucosa of the ileum and colon. The pancreas and adrenals were normal. The liver weighed 1,775 Gm., and there were slight focal fatty changes. The kidneys together weighed 290 Gm. and were of normal size; a few petechial hemorrhages were observed on the cortical surface after the capsule was easily stripped, but otherwise the kidneys, pelves and ureters appeared normal.

Microscopic Examination.—In the myocardium there was moderate fragmentation of the muscle fibers, but no nuclear changes or fibrosis appeared. In several sections peculiar hyaline masses covered with endothelium were attached to the

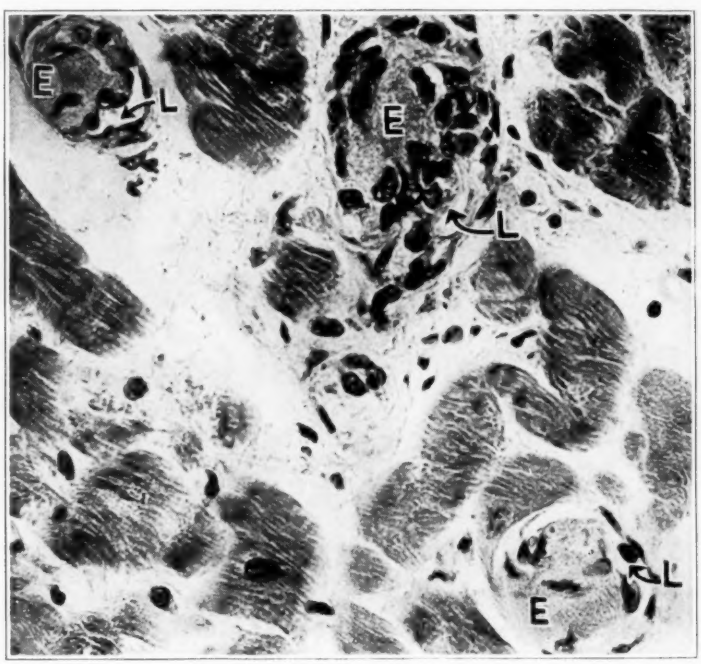

Fig. 1.—Section of the myocardium stained with eosin and methylene blue. The section shows four arterioles undergoing typical endothelial hypertrophy, with the hyaline or fibrinoid mass which intrudes on the lumen and is covered with endothelium. The obliteration of the lumen is only partial, and in each instance the lumen is pushed to the right. There is no perivascular or other inflammatory response. *E* indicates the endothelial mass and *L* the lumen.

walls of the arterioles and protruded into and blocked the lumens (fig. 1). In the kidneys some glomeruli were completely replaced by hyalinized connective tissue, and there was fusion of capillary loops. In other places fibrinous thrombosis occurred in some loops. Most capillaries were bloodless, but a few were engorged with red cells. The chief lesion was observed in the arterioles, where peculiar hyaline or fibrinoid thrombotic masses were present in the lumens, usually

fused to one side of the affected vessel and capped by proliferative endothelial cells. The medium-sized vessels showed no significant changes. The interstitium was normal in amount. The tubules showed moderate cloudy swelling. There were some hyaline and epithelial casts, and a few tubules contained red cells. The adrenals showed moderate vacuolation of the cortex; the medulla appeared normal, while the arterioles at the capsular margin showed lesions similar to those in the kidneys and heart. The pancreas contained slight interstitial deposits of fat; the parenchyma was normal, and around the arterioles were hyaline thrombi and endothelial proliferation. The spleen showed diffuse and severe arteriolosclerosis, but the malpighian bodies were intact and there were no changes in the pulp. The

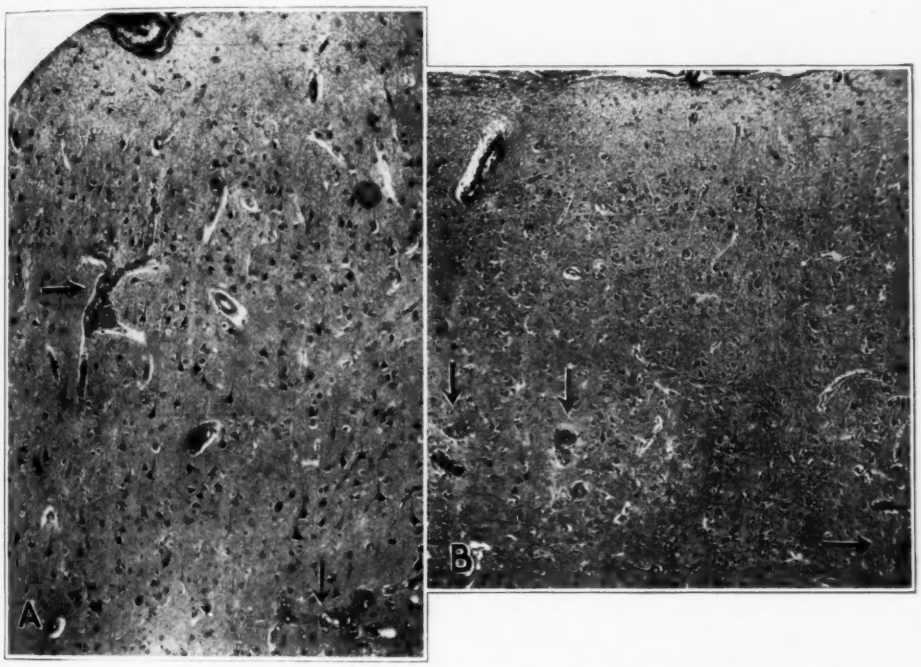

Fig. 2.—Photomicrographs of sections (*A*, stained with hematoxylin and eosin and *B*, with phosphotungstic acid hematoxylin) of the cerebral cortex including from the first to the sixth layer, showing distribution of the nodular lesions of the arterioles in from the third to the fifth layer. Arrows point to more conspicuous lesions.

liver showed moderate central fatty changes, and in some arterioles occurred the lesion present in the other organs.

The pathologic diagnosis, exclusive of the brain and cord, was: slight ventricular hypertrophy and diffuse coronary arteriolitis of the heart; early lobular pneumonia and hypostatic congestion of the lungs; slight enlargement and arteriolosclerosis of the spleen; focal fatty changes and arteriolitis of the liver; arteriolitis of the pancreas; arteriolitis of the adrenals; diffuse marked arteriolitis; focal acute glomerulitis, and cloudy swelling of the kidneys.

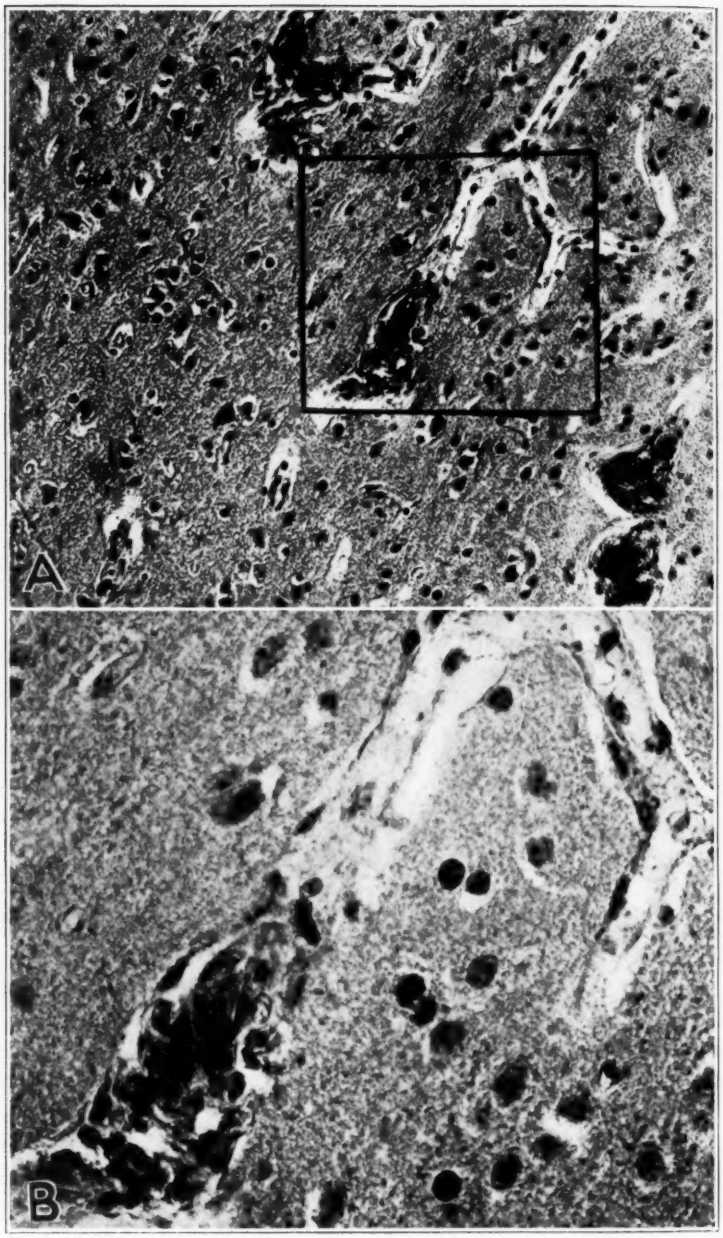

Fig. 3.—Photomicrographs of sections from the fourth layer of the motor cortex stained with phosphotungstic acid hematoxylin. *B* shows a higher magnification of the central part of the field shown in *A*. In *A* five different knotlike lesions are seen on the arterioles. It may be noted that the swelling along the course of the vessel is composed of hypertrophied and necrotic endothelial cells. There is also diffuse hypertrophy of the endothelial cells along the course of the small vessels above the point of the lesion.

Brain: Grossly the brain appeared to be of natural size and coloring. The cut surfaces also appeared normal.

Microscopic studies were made on sections taken from various areas of the cerebral cortex, the cerebellar cortex and several levels of the brain stem and stained with hematoxylin and eosin, van Gieson's stain, Mallory's phosphotungstic acid hematoxylin stain for elastic tissue, Loyez' myelin sheath stain, Nissl's stain, the Hortega silver stains for neuroglia and microglia and the sudan III stain for fat.

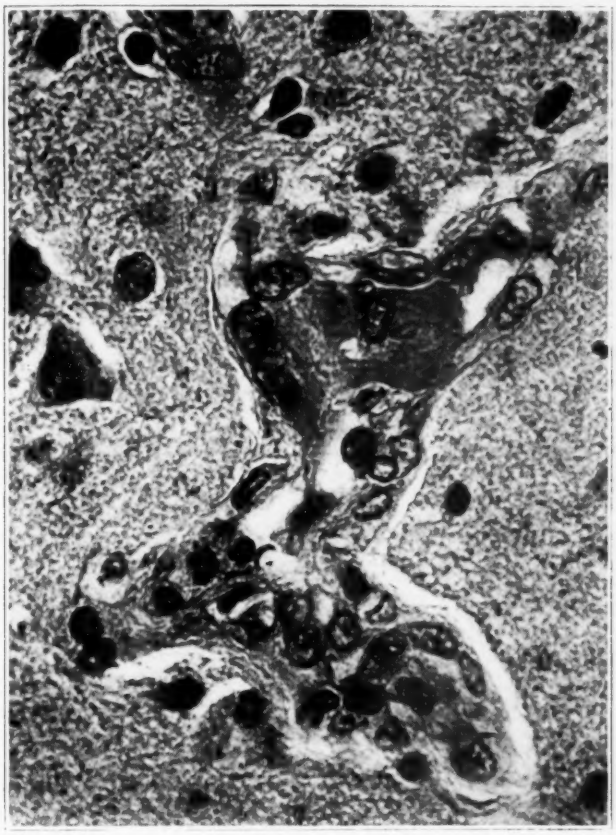

Fig. 4.—Photomicrograph with high magnification of one of the lesions in an arteriole of the cerebral cortex. The normal arteriole on the right expands into the knotlike mass of endothelial cells, with degenerating products which invade the lumen of the vessel.

In the cerebral cortex the meninges, including the pia and all the larger blood vessels, were normal. The first layer of the cortex and the subcortical white tracts were normal. However, in all cortical areas studied a typical lesion was located in the deeper layers of the cortex, especially from the third to the fifth layer, and was characterized by vascular and parenchymal changes. One obtained the impression that the vascular change was primary, as this lesion was the same

as that in the smaller vessels of the myocardium, kidneys and other organs, as well as in other parts of the brain. Characteristically the lesion was an endothelial thickening of the small arterioles or capillaries. It usually occurred at the point where the smaller vessel branched from the tree. It was therefore usually nodular, although a more moderate amount of endothelial proliferation was shown along the course of many smaller arterioles and capillaries. As shown in figures 2, 3 and 4 several of these nodules were formed in the arterioles of from the third to the fifth layer of the cerebral cortex. Figure 4 shows a high power view of a nodule. The nodule was formed from endothelial proliferation, which tended to occlude the lumen of the vessel and enlarge its diameter, like a knotty growth. The endothelial cells first became swollen and succulent and proliferated. The cells became necrotic, with a hyaline background and a granular matrix. With phosphotungstic acid hematoxylin the hyaline substance stained red and the granules blue. It has been suggested [5] that these two substances were formed, respectively, from the cytoplasmic and the nuclear residual material of the necrotizing endothelial cells. The granular mass tended to plug the vessel but was always surrounded by the outer endothelial membrane so that it did not appear to be formed from substances that are derived from the blood stream. The stain for fat showed lipoid pigment in some of the more active endothelial cells or in those nearest the proliferating cells but not in the center of the necrotic mass. There was also lipoid in the few perivascular cells. Paling of the larger ganglion cells and increase in the satellite glia cells and rod cells were also shown with the Nissl stain. A silver stain showed a marked increase in the spider glia cells with pedal attachments to the walls of the vessels, especially in the areas in which the vascular lesion was prominent (fig. 5). The microglia cells were not increased. Occasional petechial hemorrhages were seen, apparently due to diapedesis. There was no demyelinization or inflammatory reaction anywhere in the brain.

In the cerebellum the lesion was also of characteristic form and location. The pia and pial vessels were normal. As the small arterioles left the pial vessels and passed through the molecular layer there was diffuse endothelial swelling. At the layer of Purkinje cells, where the arterioles tend to branch into capillaries, the nodular vascular lesion was frequent. Figure 6 shows a microscopic view of a cerebellar lobule, with several nodular lesions in the arterioles in the layer of Purkinje cells. Figure 7 *A* shows an arteriole passing through the molecular layer in which a nodular lesion of this type is fully developed at the level of the Purkinje cells. At this point the proliferation of the endothelial cells is evident, with a granular mass that occludes the lumen of the vessel. It is seen, however, that the lumen (to the right) passes lateral to the mass. Figure 7 *B* shows another section of the cerebellum in which the arteriole divides into three capillaries just beyond the layer of Purkinje cells; at the point of division there is a necrotic endothelial nodule involving each capillary. Surrounding these nodular masses there are loss of the cerebellar granular cells and replacement with spider glia cells.

In the brain stem the same vascular lesion was seen in the large nuclear masses, such as the olive, the pontile nuclei (fig. 8), the nuclear masses about the ventricles and the basal ganglia and thalamus. The white tracts did not show the lesion, but even where a relatively small nuclear mass was surrounded by white tracts, as in the pons, the gray masses usually showed the nodular vascular lesion at the point where the vascular bed breaks into the network of branches, and the white tracts were free from involvement. There was also noticeable productive ependymitis throughout the ependymal system.

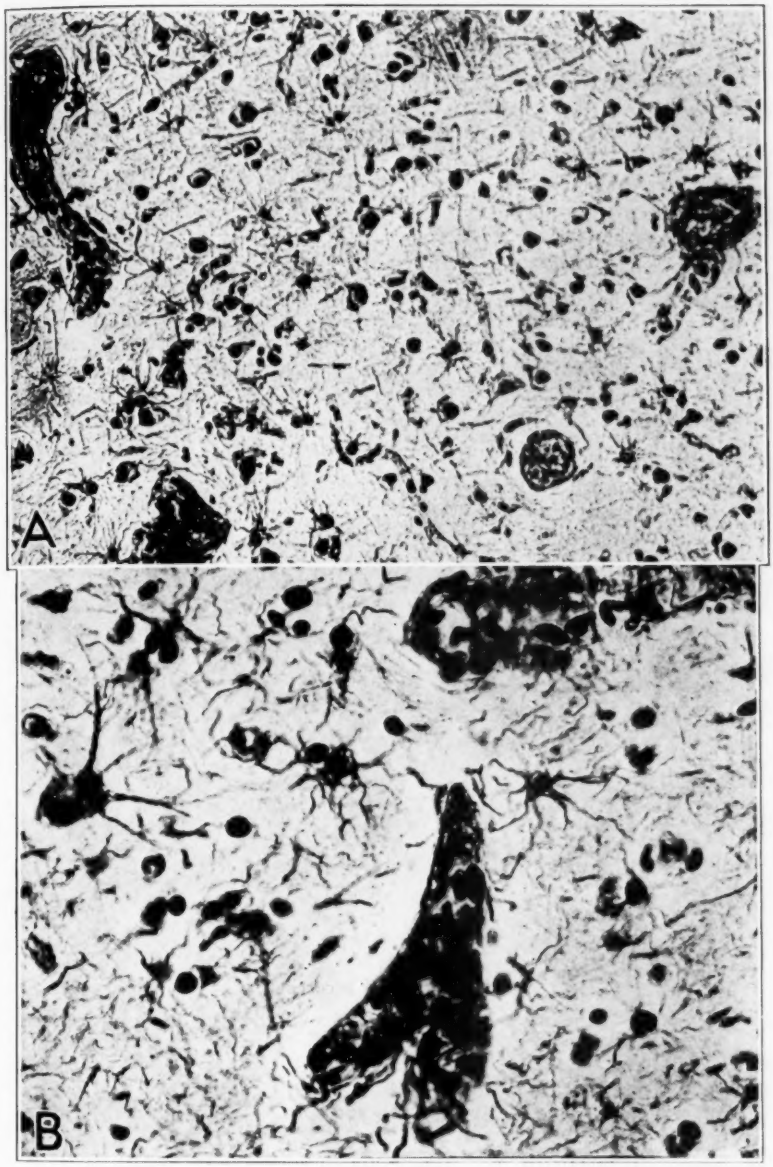

Fig. 5.—Photomicrographs of sections of the motor cortex stained with Hortega's silver stain for neuroglia. *B* is taken with a higher magnification than *A*. Both show several knotlike lesions in the arterioles and proliferation of the neuroglia cells about the lesions on the vessels and in the surrounding tissue. The astrocytic, spider-like neuroglia cells with their pedal connections with the walls of the blood vessels are clearly seen.

The diagnosis on the basis of the cerebral histopathologic picture was subacute disseminated arteriolitis of the brain.

In summary the observations in this case lead one to suppose that this man had suffered from a subacute infectious process of six or eight weeks' duration, associated primarily with pneumonia and secondarily with disseminated arteriolitis of the myocardium, kidneys and other viscera and of the brain, with associated disturbances in the psychic, neurologic, cardiovascular and renal functions, and progressive anemia. This case is the first instance of this disease in which the psychic, neurologic and cerebral changes have been described and correlated with the rest of the disease process.

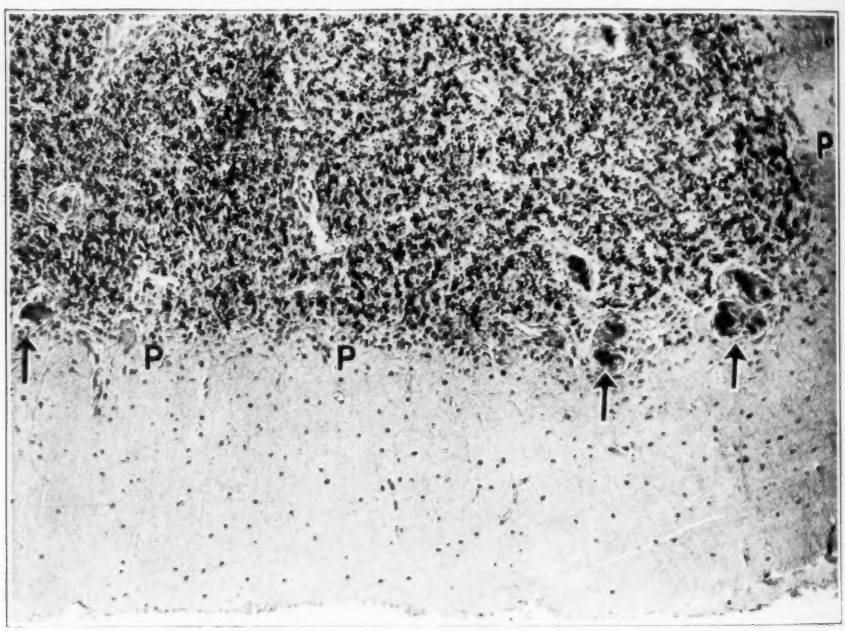

Fig. 6.—Photomicrograph of a section of a cerebellar lobule, showing a number of knotlike lesions in the arterioles in the layer of the Purkinje cells. Arrows point to the more conspicuous lesions. *P* indicates Purkinje cells. Phosphotungstic acid hematoxylin stain.

CASE 2.—*History.*—D. W., a Negress, aged 28, who suffered from postabortal sepsis, was transferred to the psychiatric pavilion of the Bellevue Hospital on April 13, 1934, from another city hospital, because she was confused, had hallucinations and was uncooperative. The history given by her husband was that she had had an abortion induced some time in January, when she was four and a half months pregnant. She seemed to recover and returned to work but gradually became weak and sick and could not keep anything on her stomach; a foul vaginal discharge developed. A private physician was called on April 6 and reported that he found a dirty brown discharge and enlargement and tenderness of the uterus,

with pain in the lower abdominal quadrant on both sides; the temperature was 100 F., the pulse rate 112 and the blood pressure 140 systolic and 90 diastolic. The urine contained no albumin or sugar but was loaded with pus cells. The condition seemed to improve with treatment, until severe pain suddenly developed in both lower quadrants of the abdomen. She was taken to a city hospital, where she remained only one day because she became delirious. She was transferred to the Bellevue Hospital.

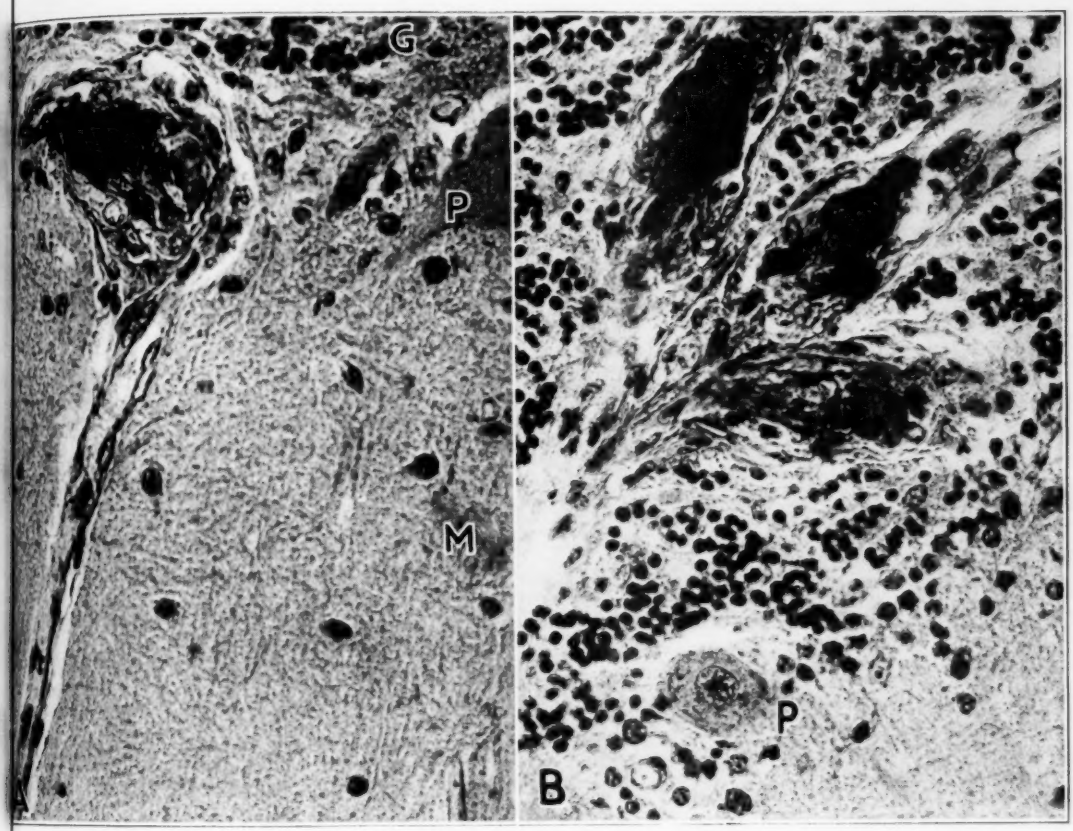

Fig. 7.—Photomicrographs of sections of the cerebellum stained with phosphotungstic acid hematoxylin. *A* shows a hypertrophied arteriole arising from the pia (below) and passing through the molecular layer (*M*) of the cerebellum to the layer of Purkinje cells (*P*). In the upper part of the picture is shown the beginning of the granular layer (*G*). The knotlike endothelial growth in the endothelial lining of the arteriole is seen just as it reaches the layer of Purkinje cells, where it divides into capillaries. In the center the granular necrotic mass is surrounded by the swollen endothelial cells, which are pushed toward the lumen. *B* shows an arteriole arising from the molecular layer in the lower left corner which divides into three capillaries, and at this point there is formed the granular, cellular endothelial mass in the course of the vessels.

Examination.—At the time of admission the patient was confused, disoriented and apprehensive. She said: "I only knew her. Why should I try to do anything bad about her? Maybe somebody else. And all those things; where did they come from? They have other people besides me. I didn't know where I was going. You know I have nothing against these people. I don't know what place this is, but I am afraid of him. I want him to keep quiet." On the next day she was less rambling and gave an account, somewhat incoherent, of her delirious episode in the other hospital. She was still fearful, bewildered, confused and uncooperative. She said: "I am so sick; you don't understand, lady. I went to the hospital Tuesday. I am so blank now—Tuesday or Wednesday. They took me to St. Vincent's Hospital [not true], it was supposed to be. But they all grabbed me in such a queer way. It wasn't a hospital. The nurses weren't real nurses. The next day they had cops and things looking around. At 6 o'clock in the

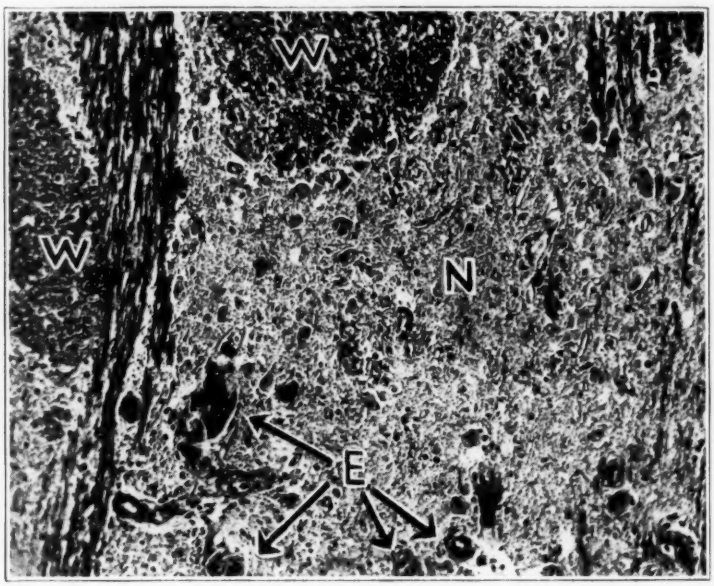

Fig. 8.—Photomicrograph of a section of the brain stem at the level of the pons, stained with Mallory's phosphotungstic acid hematoxylin, showing areas in the pyramidal tract (*W*), which have no vascular lesion and areas in the pontile nucelar masses (*N*), which show numerous lesions. Especially in the lower right corner are a number of these endothelial proliferations (*E*) at the point in the course of the vessel where it divides into the smaller units.

morning they had a group of them running around, beating heads. I was really delirious. We didn't have a nurse or doctor for two hours. When they came, they had been fighting. I think it must have been gangsters. Please take me to a hospital. I am afraid of this place. No, I can't eat; my lips are all parched from the poison they gave me. I wish you would find out. I don't understand it at all."

The patient was poorly nourished and dehydrated and appeared toxic; the conjunctivae were injected, and the lips and tongue were dry. The heart and lungs were normal. The abdomen was flaccid, with tenderness in the pelvic area on

both sides. The breasts were atrophic. Neurologic examination gave normal results. Vaginal examination was unsatisfactory because of poor cooperation, but nothing abnormal was detected. The temperature at this time was normal; the pulse rate was 88, and the blood pressure was 114 systolic and 76 diastolic. The Wassermann reaction of the blood was negative. Urinalysis showed albumin (2 +) and many pus cells, with clumping.

Course of Illness.—After a few days the patient's mental condition improved, and she remained clear and cooperative until the appearance of terminal coma. She seemed also to improve physically for a few days, but on April 19 she was much worse. The mucous membranes were dry, and she displayed a generalized erythematous papular rash. The abdomen was tender, especially in the lower quadrants. The urine contained albumin (2 plus), with many pus cells and clumping, and the specific gravity was 1.008. The temperature had risen, with

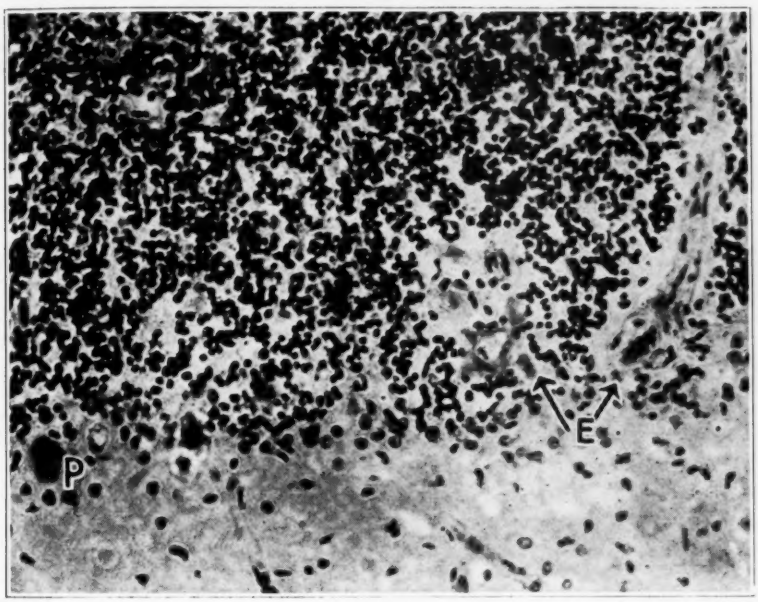

Fig. 9.—Photomicrograph of a section of the cerebellar cortex in case 2, showing the molecular layer in the lower part of the picture and the granular layer in the upper part, with the Purkinje cell layer (*P*) between them. On the right an arteriole (*E*) arising from the molecular layer divides into two capillaries at the level of the layer of Purkinje cells and shows endothelial proliferation, with diminution of the surrounding granular cells and replacement with astrocytes.

several peaks, to 101 and 102 F. The pulse was relatively more rapid, the rate ranging from 130 to 140 beats a minute. The blood pressure had risen sharply to 200 systolic and 140 diastolic.

After this there were several nosebleeds and progressive anemia. Treatment with fluids and methenamine and di-sodium hydrogen phosphate was administered, and after a few days the urine was free from pus cells and albumin, but the pulse rate remained from 130 to 140 a minute. The vaginal discharge increased, with abdominal rigidity. A blood culture on May 2 was reported sterile. The blood pressure was then 200 systolic and 114 diastolic. The nonprotein nitrogen content

of the blood was 117 mg. The urine had a specific gravity of 1.010. The erythrocyte count was 3,050,000, with 70 per cent hemoglobin; the leukocyte count was 11,470, with 81 per cent polymorphonuclear cells. The eyegrounds showed marked neuroretinitis, with flame-shaped hemorrhages and patches of whitish exudate.

The tentative diagnosis was that of sepsis following abortion, with pyelonephritis or subsequent glomerular nephritis and secondary hypertension and uremia. An icteric tinge of the scleras was noted, and the van den Bergh reaction was positive to both the direct and the indirect test. The icteric index was 1.65, suggesting that the jaundice was probably the result of necrosis of liver cells.

On May 7 the patient became dyspneic and edematous and showed neurologic deviations. She lay quiet and made slow, purposeless movements of both arms. The eyes rotated upward and to the left. The pupillary responses were normal. There were no muscular twitchings. The tendon reflexes were normal. She passed into a state of coma and died that night.

Gross Postmortem Examination (May 8, 1934).—The body was slender. There were slight pitting edema of the lower extremities and a diffuse punctate eruption on the anterior abdominal wall. The peritoneum was dry and smooth; there were 800 cc. of straw-colored fluid in each pleural sac, with no adhesions, and a slight excess of fluid in the pericardial sac. The heart weighed 410 Gm.; the left ventricle was hypertrophied; otherwise, there were no intrinsic changes. The visible coronary vessels showed occasional eccentric atherosclerotic plaques. The aorta was smooth and elastic, showing a few atheromatous plaques in the abdominal portion. There were slight emphysema of the lungs and edema and compression atelectasis of the lower lobes. The gastro-intestinal tract showed no changes except a nodular swelling, 3/16 inch (0.47 cm.) in diameter, on the posterior surface of the stomach. The pancreas, adrenals, gallbladder and bile ducts were normal. The spleen was small, weighing 80 Gm.; it was soft on section, and the follicles were indistinct. The kidneys together weighed 260 Gm.; the left was slightly larger than the right; the capsules stripped easily, leaving a moist surface, and the surface of the left kidney was faintly granular and was studded with pinpoint hemorrhages. The renal pelves and ureters were normal. The uterus showed a small interstitial fibromyoma and adhesions to the adnexa. No placental site was discovered, and there was no evidence of endometritis.

Microscopic Examination.—The heart presented mild hypertrophy of the nuclei and fibers and mild coronary sclerosis. The aorta showed atherosclerosis. One section of the lung showed an early stage of sublobular inflammatory exudate, consisting of fibrin and polymorphonuclear and red cells; heart failure cells and edematous fluid were also seen in other sections. In the liver there was marked congestion, with dilatation of the coronary vessels and pressure atrophy of the adjacent cords. The stomach showed no vascular lesions. In the pancreas many arterioles and several small arteries revealed sclerosis and focal fibrinoid necrosis. The adrenals displayed arteriosclerosis. Examination of the kidneys revealed that the majority of the glomeruli were intact and ischemic; a number showed mild simplification of the loops, and a few were reduced to hyaline spheres; an impressive minority exhibited fibrinoid necrosis of the glomerular loops, varying from a single focal capillary lesion to necrosis of the entire tuft; hemorrhages were present in the capsular space in a few instances; the arterioles were uniformly markedly thickened, and many showed fibrinoid necrosis of the walls; larger vessels showed moderate sclerosis, with marked reduplication of the internal elastica, and the tubules showed no notable change other than the presence of occasional red cells; the interstitium was not fibrotic; occasional focal infiltration

with lymphocytic cells was seen, and in one field of a section a zone of fresh hemorrhagic infarction was noted. Sections of skeletal muscles revealed that the walls of several arterioles exhibited fibrinoid changes.

The pathologic diagnosis, exclusive of the brain and cord, was: Moderate arteriolonephrosclerosis, with widespread necrotizing arteriolitis and punctate hemorrhages of the kidney; hypertrophy of the left cardiac ventricle, slight sclerosis of the mitral valve and coronary arteriosclerosis; early sublobular pneumonia and chronic passive congestion of the lungs; bilateral hydrothorax; chronic passive congestion of the liver; arteriosclerosis and focal necrotizing arteriolitis of the pancreas; congestion and edema of the wall of the bladder; recent fibrous adhesions of the right uterine tube, ovary and uterine fundus, with a small intramural fibromyoma; milk in the breasts; generalized anemia of the organs, and moderate edema of the lower extremities.

Brain: Grossly there were congestion on fresh section and thickening of the walls of the larger vessels; otherwise the brain appeared normal.

Microscopic studies were made of sections from areas of the cerebral and the cerebellar cortex, the floor of the fourth ventricle with the overlying lingula and the floor of the third ventricle with the mamillary bodies, which were stained with hematoxylin and eosin, Van Gieson stain and phosphotungstic acid hematoxylin.

In the cerebral cortex there was thickening of the walls of the large and small arteries and the arterioles, characterized by increase in the cellular elements of the intima and media but especially by endothelial proliferation of the smaller arterioles. There was also an endothelial increase in the pia. The small arterioles that penetrate the cortex from the meningeal surface showed especially the endothelial hypertrophy, and this was particularly evident in the arterioles of the deeper layers of the cortex. There was slight endothelial thickening of the larger vessels of the subcortical areas as well. The vascular proliferation was not uniformly present but occurred in patchy areas. Occasionally small hemorrhages due to diapedesis were seen. In the cerebellar cortex the pia and the vessels of the meninges showed the same kind of endothelial hypertrophy. The small arterioles, as they penetrated the molecular layer, showed endothelial proliferation, but this was especially conspicuous in the Purkinje layer (fig. 9), where in places small knotlike processes were seen on the arteries as they divide into capillaries, with endothelial increase and swelling of the vessel. There was diminution of granular cells immediately around a budlike lesion of a vessel of this type, with increase in astrocytic glia cells. About the third and fourth ventricles the larger vessels showed hypertrophy of the internal cellular elements, with edema in the perivascular space. The parenchyma in all places appeared intact; the nerve cells were normal, and there were no inflammatory processes.

The diagnosis on the basis of the cerebral histopathologic picture was diffuse arteriosclerosis of the larger cerebral and meningeal vessels and patchy arteriolitis, especially of the cerebral and cerebellar cortex.

COMMENT

Clinical and General Pathologic Condition.—The question of the clinical entity and etiology and the general pathologic problem in relation to disseminated alterative arteriolitis will not be discussed in detail. Suffice it to say that the two cases reported are somewhat similar to the one reported by Strang and Semsroth,[8] in which alterative, productive and obliterative arteriolitis of the myocardium and kidneys occurred,

with slight valvular excrescences associated with low grade streptococcic infection. The condition may be accounted for by the low virulence of the organism and the high reactive power of the reticulo-endothelial system of the organs of the body. If one considers a series in which the most acute process is represented by acute bacterial endocarditis, with severe inflammatory reaction of the valves of the heart and other parts of the vascular bed, and then considers the different grades of subacute bacterial endocarditis, rheumatic endocarditis and the indeterminate type of Libman and Sacks, in which the excrescences of the valves of the heart and the responses of the endocardium and vessels of the heart and kidney (with nephrosclerosis) become more productive of endothelial cells and are less of the inflammatory type, one finally comes to the least acute process, with low grade infection and an endothelial response which is more or less limited to the smaller network of the arterioles and the capillary bed and in which the lesion is essentially one of productivity of the endothelial elements, with granular necrosis and obliteration of the lumens of the vessels and secondary failure of the blood supply to the vital organs. This is the clinical and pathologic picture presented in the two cases reported in this paper. In neither case was any productive or inflammatory process demonstrable in the valves of the heart or the endocardium; the lesion was restricted to the vascular beds of the organs—in case 1, to the smaller arterioles and capillaries, and in case 2, also to the larger vessels of the organs and some other endothelial tissues, such as the pia. In case 1 the clinical course was one of low grade infection, of undetermined type, which produced confluent terminal pneumonia and disseminated arteriolitis, involving especially the heart muscle, kidneys and brain. There was progressive anemia, with a terminal rise in blood pressure and dilatation of the left ventricle, but the important clinical symptoms pointed toward the cerebral pathologic involvement. Case 2 was one of subacute septicemia following an abortion, and at the termination evidence was given of progressive failure of the cardiovascular, renal and hepatic systems, with rise in blood pressure, increase in the nonprotein nitrogen content of the blood, jaundice, edema and dyspnea.

Neurologic Status.—Neurologic signs in case 1 were prominent from the time of the patient's admission to the Bellevue hospital. They suggested a diffuse cerebral lesion, and a diagnosis of toxic encephalitis of unknown origin was offered before death. The neurologic signs suggested lesions of the cerebrum, cerebellum and brain stem, and the retinas showed vascular disturbance and blurring of the disks. The generalized type of disturbance is of particular interest in view of the disseminated form of the lesion, which was most prominent in the arterioles and capillaries that feed the nuclear masses of the brain stem, the Purkinje layers of the cerebellum and the deeper layers of the cerebral

cortex. The prominent symptoms related to involvement of the cerebral cortex were the psychic changes, which will be discussed under a separate heading, the spastic signs, at times unilateral, with reduction in sensibility to painful stimuli, and the terminal coma; the dysmetria, ataxia, adiadokokinesis and nystagmus (without other ocular signs) were related to lesions in the cerebellar cortex, and the dysarthria and disturbances in motility, consciousness and vegetative functions, to involvement of the brain stem.

In case 2 the neurologic signs were less prominent until termination with coma, purposeless movements of the limbs and rotation of the eyes.

Psychiatric Status.—Case 1 is of special interest. Psychomotor retardation was reported from the time of the patient's admission to the first hospital and led to a diagnosis of toxic encephalitis. Hallucinatory experiences, especially visual but suggesting vestibular components (Schilder [25]), were present early, without much confusion. A prominent and interesting symptom was the belief that the concept of time had changed—that time took too long. Mach [26] has claimed that the concept of time is related to the rate of blood flow through the brain. Consequently, a disease process that obliterates the lumen of the smaller vessels just as they break into the capillary bed would tend to slow the blood flow through the cortical layers and interfere with the normal concept of time. Of course, this is hypothetic, and the vascular change is certainly not the only factor concerned in disturbances of time perception, which occur commonly in many toxic states, such as in marihuana intoxication (Bromberg [27]). Gradually, disorientation in time and place developed in this case, with rambling, disconnected thought processes, poor attention, difficulties in perception and inadequate comprehension of the situation, with perplexity, which Schilder [28] showed to be the central manifestation in the acute confusional states associated with toxic and organic disease of the brain. The disturbance in consciousness and coma represent the final stage and are associated with the disseminated lesions both in the cortex and in the brain stem, as shown by Bender and Schilder [22a] also in cases of alcoholic encephalopathia.

In case 2 the cerebral changes were less severe and were associated with a transitory period of delirium, with confusion, perplexity and

25. Schilder, P.: The Vestibular Apparatus in Neurosis and Psychosis, J. Nerv. & Ment. Dis. **78**:1, 1933.

26. Mach, E.: Beiträge zur Analyse der Empfindungen, Jena, Gustav Fischer, 1886.

27. Bromberg, W.: Marihuana Intoxication, Am. J. Psychiat. **91**:303, 1934.

28. Schilder, P.: Introduction to a Psychoanalytic Psychiatry, translated by Bernard Glueck, Nervous and Mental Disease Monograph 50, Washington, D. C., Nervous and Mental Disease Publishing Company, 1928.

hallucinations, and a terminal period of deep clouding of consciousness and coma.

Neuropathologic Status.—The lesion is a specifically localized vascular one, characterized by endothelial swelling and proliferation, which tends to obliterate the lumen of the vessel and increase the size of the vessel. The swollen endothelial cells appear to break down into a necrotic, granular hyaline mass, which is composed of the nuclear and cytoplasmic substance of the hypertrophied cells. It gives the appearance of a central granular plug within the swollen endothelial cellular mass, but there can always be seen the remnants of a free lumen within the endothelial membrane, so that the plugs appear not to be thrombotic; that is, they seem to arise not from the blood stream but from the endothelial walls of the vessels, and the lesion is therefore more of the nature of a knot, or endothelial granuloma, than of a plug. There may be a slight diffuse endothelial swelling for some distance along the smaller arterioles and capillaries, but, in addition, there is a characteristic nodular swelling, which occurs just at the point where the arterioles divide into capillaries. This is the most typical part of the lesion in the brain. It has a special localization in the brain which is related to the angio-architectonics of the brain. Wherever the arteriolar bed breaks sharply into a capillary network the knotlike lesions on the vessels are most numerous. Therefore, they are observed in the cortex most commonly in from the third to the fifth layer, in the cerebellum in the Purkinje layer and in all parts of the brain stem where a gray nucleus is surrounded by white tracts. In other words, this lesion occurs in the parts of the central nervous system which are richest in the supply of capillaries, or in all the richly cellular groups of nerve cells. The parenchyma suffers secondarily, either from interference with the blood supply or from the same toxic disturbance that causes the vascular lesion. There is, however, no inflammatory process, but there are diminution in the immediate nerve cell content, paling of the larger nerve cells and increase in the astrocytic glia cells. This characteristic lesion was best shown in case 1; in case 2 a similar process was shown, which was less pronounced and was superimposed on generalized endothelial hypertrophy, some hypertrophy of the media of the large and small vessels and endothelial hypertrophy of the pia. In case 2 the generalized vascular changes may have been related to the hypertension. In general, the cerebral pathologic picture of the cerebrum is only a part of that of the whole body. The same type of disseminated alterative, productive, necrotic arteriolitis is present in all organs of the body and is associated in each organ with its own peculiar type of organic response and failure. In case 1 the cerebral involvement was the most marked, and in case 2 the cardiovascular, renal and hepatic involvement was the important feature.

SUMMARY

Two cases of disseminated alterative, productive, obliterative arteriolitis are described. The concept of this disease entity has evolved from that of acute bacterial endocarditis, in which an infectious agent produces a productive and destructive lesion of the whole inner lining of the cardiovascular system, with typical vegetative endocarditis in the more acute forms. Less acute processes occur in rheumatic endocarditis, subacute bacterial endocarditis, and the so-called Libman-Sacks disease, which is of neither rheumatic nor bacterial origin but in which there is productive verrucous endocarditis, with more or less endothelial proliferation through all other parts of the vascular bed. This process, being less inflammatory and less destructive, is said to be a response of the host to the toxic products of the infectious agent rather than to the virus itself, though this has not been proved. The two cases reported in this paper are instances of apparent infection, one associated with a pulmonary process and the other with an abortion, in which lesions of the heart valves and walls were not detected but in which the productive arteriolitis was present in the myocardium and in all internal organs, including the brain. No similar studies of the brain have been made. The cerebral lesions were like those in other organs of the body and were characterized by endothelial proliferation, swelling, necrosis and obliteration of the lumen. This endothelial hypertrophy occurred especially as a knotlike process at the point where the arterioles break into the capillary network. It had a characteristic localization in the central nervous system in the larger groups of nerve cells, especially from the third to the fifth layer of the cerebral cortex, the Purkinje layer of the cerebellum and the well organized nuclei of the brain stem. The vascular lesions were associated with secondary loss or paling of the nerve cells and proliferation of the astrocytic cells and with typical neurologic and psychic disturbances related to the failure in function of the cerebral and cerebellar centers and those of the brain stem. The lesions and the secondary organic failure were progressive; in case 1 death was due apparently to cerebral failure, and in case 2, to cardiovascular, renal and hepatic failure, with associated cerebral signs.

Technical and Occasional Notes

EFFECT OF BENZEDRINE SULFATE ON MOOD AND FATIGUE IN NORMAL AND IN NEUROTIC PERSONS

ABRAHAM MYERSON, M.D., BOSTON

Drugs that affect mood are few. Alcohol produces in many persons euphoria which is followed by depression, although the changes in mood brought about by alcohol are so diverse as to give rise to the famous aphorism *in vino veritas,* meaning that the true underlying mood of the person comes out while he is drunk. Narcotics deaden the personality and thus bring about an escape from an intolerable mood. The anesthesia of mood which is sought and obtained by this means is purchased at an enormous price, so far as personality worth is concerned.

Caffeine, in the form of tea and coffee, has a place in the daily habits of the human being largely because of the mild toning-up process which takes place. In most instances the use of drugs to banish fatigue and depression has little to recommend it except in the case of strychnine and caffeine.

I have utilized benzedrine sulfate to relieve the fatigue experienced by the normal person after an insufficiency of sleep. It may be stated categorically that in at least a dozen persons who were given this drug for this purpose the effect was, without exception, quickly felt and apparently prized. A dose of from 5 to 20 mg. of benzedrine sulfate, taken by mouth, causes a warm glow which is agreeable and which is associated with a sense of relaxation and, at the same time, disappearance of the tired feeling around the face and eyes, which is perhaps the most disagreeable consequence of insufficient sleep and rest. The effect lasts, by introspection, from two to several hours. One tablet of 10 mg. is usually sufficient to produce this result. If three tablets are taken the subject may feel "jittery"; that is, he has a sense of overtension and some excitability. On the other hand, a moderate dose produces a sense of calm which is gratifying.[1]

It is the universal experience of normal subjects that if the drug is taken in the late afternoon sleep becomes difficult to obtain and may be banished. I have experimented on myself on three occasions and have found that after taking the drug I have stayed awake all night, but without the usual restlessness of insomnia.

From the Division of Psychiatric Research, Boston State Hospital, Mattapan, Mass.

This study was aided by grants from The Commonwealth of Massachusetts and the Rockefeller Foundation.

1. Since writing this paper I have come definitely to the conclusion that the giving of small doses, with no more than 5 mg. as an initial dose and perhaps a total of from 10 to 15 mg. in the morning, is the best method of administration of the drug to neurotic persons for amelioration of mood.

Whether the effect in normal persons would be maintained if the drug were taken regularly each day, I cannot state. It is probable that the effect would wear off and that the drug is valuable to normal persons only as a measure to be used for emergency purposes. No ill effects have ever been noted in any of our cases, and there is no rise in the blood pressure of any consequence when 10 mg. is taken. With 20 mg. there may be some rise, which would contraindicate the use of the drug by elderly persons with hypertension. None of our normal subjects complained of any ill effect, and none of them experienced any craving for the drug afterward. All agree that to dissipate the "hang-over" of a disordered night's sleep or of insufficient rest the use of the drug is worth while.

RESULTS IN PERSONS WITH NEUROSES AND DEPRESSIVE STATES

Benzedrine sulfate was given extensively for the past six months to persons suffering from neuroses of various types. Results of treatment in persons with neuroses are difficult to evaluate. There are many instances of spontaneous recovery and improvement. The conditions run such a variable course and so many diverse technics are of apparent therapeutic value that to link any therapeutic agent with the result that appears to follow is at present almost impossible. This is attested by the fact that quite different approaches are reported to be of value, ranging from psychoanalysis to physical therapeutics and including the extramedical methods of osteopathy, chiropractic, Christian science, faith-healing and the like.

The truth is that marked remission and exacerbation occur spontaneously in these conditions, and the vagueness of knowledge concerning the conditions makes any scientific evaluation of results difficult. Benzedrine sulfate seems to have definite though limited value in combating the neuroses. It can be definitely stated to be an ameliorative agent rather than a curative one; that is, when used judiciously it is of value in lessening the distress and the depression and increasing the feeling of energy. There seem to be no ill effects in the majority of instances if a dose is administered in proper relationship to the time of sleep.

The following brief case histories illustrate the results obtained.

CASE 1.—D. F., a man aged 52, has for twenty years had a morning depression, at which time he has a feeling of extreme weakness and marked depression, with agitation and a suicidal urge. In the afternoon his personality trends come back nearly to normal; he is not depressed, feels moderately vigorous and has the desire to do work, and his appetite returns. A difficulty common in such conditions appears toward night, in that he becomes somewhat too excited to sleep.

The family history indicates that this condition is a minor form of manic-depressive psychosis, as two members of his immediate family have committed suicide.

With the onset of the financial depression he lost his position as an engineer, and from that time on his day was divided into two parts: In the morning his personality was altered—he was restless and agitated, had no desire to meet others and felt a deep inferiority when he came in contact with them and had an urge to commit suicide, which he called a "death wish" and which gave him and his wife

great concern. In the afternoon his condition was that already described. He has been under my care for about a year, after having been treated by a number of of neurologists and psychiatrists without noticeable results.

The use of strychnine and caffeine in the morning to lift him out of his mood and the administration of sedatives at night brought about a moderate degree of amelioration in that sleep was restored, but the morning depression, although somewhat lessened, was still severe enough so that he could do no work, and he still had the death wish.

Four months ago the use of benzedrine sulfate was started. He was given 20 mg. on arising and from 10 to 20 mg. at about noon. He kept notes on his condition from that time on. These eloquently attest that the morning depression disappeared until about 10 o'clock; then the administration of another dose of the drug relieved him again until afternoon. The death wish became so attenuated that it did not trouble him. He was able to do work in the morning; the afternoons remained as comfortable as before. In many notes he stated substantially that there was no sense of increased tension or excitability, as was the case when he took strychnine and caffeine, but the feeling was as though a toothache had disappeared, leaving a sense of peace and quiet. When the dose of benzedrine sulfate was diminished the same results were not obtained. There was only a moderate amelioration of the symptoms. When sugar of milk was administered as a placebo the former symptoms returned. On several occasions he came to the laboratory without having taken the drug in the morning. At such times he was exceedingly agitated and depressed; his face was anxious and his voice quavery, and a general attitude of despondency was demonstrated. The administration of 20 mg. of the drug dissipated most of the emotional disturbance within twenty minutes. During this time his sexual appetite, his desire for food and his bowel movements and general visceral functions were unimpaired. His blood pressure was not raised by the use of benzedrine sulfate and there was no effect on the heart. This effect has continued consistently throughout the period of experimentation, without any apparent loss of potency.

Case 2.—L. McL., a woman aged 40, a school teacher, had a severe emotional reaction with a neurosis following divorce. There were many complicating social and sexual disturbances. She showed moderate improvement and then had a serious automobile accident, as a result of which an extreme anxiety neurosis developed. There were a marked hysterical tremor of the right arm and a sense of low energy, with general depression of the appetite, power to sleep and capacity for mental and physical work. She reached a point where, in order to overcome her depressed state, she drank as much as ten cups of coffee a day, despite the admonition of the physician. This condition continued, with some ups and downs, for nearly ten months. Whatever improvement took place was in respect to the tremor of the right arm, which gradually became less marked. She took a sedative at night to produce sleep, since on those occasions when she omitted the barbital she would lay awake all night and was in a deplorable state the next morning.

Two months ago the use of benzedrine sulfate was started, two tablets being given in the morning and one at noon. Within a day the sense of fatigue in the morning and the extreme depression almost disappeared. She discontinued the use of coffee, since she felt that she no longer needed it. Her mood improved correspondingly. She took a trip and returned home feeling well enough to return to work and is now back at work as a school teacher. Under the stress of work she has become fatigued again. Although the fatigue is by no means extreme, with two extra days a week off she is showing definite improvement.

The temporal relationship of the improvement to the use of benzedrine sulfate is striking. She has refused to discontinue the use of this preparation, stating that when she has omitted it for a day there has been a return, in lesser degree, of the depression and the feeling of disorganization.

CASE 3.—B. B., a youth aged 18, has seemed to me to have an early stage of dementia praecox. Nevertheless, the diagnosis is uncertain. The patient has within the past year or so shown retreat from activity, complained that his eyes and head felt tired and shown confusion and inability to carry on his work. There have been a lowered interest and pronounced hypochondriasis. His whole life has been characteristic of the shut-in personality, with auto-eroticism and complete lack of heterosexual activity. There is a block in his answers which tend to be fragmentary. There are, however, no delusions or hallucinations. He can be aroused to relevant and coherent answers. He remained in this condition for about a year despite the use of various therapeutic agents.

A month ago benzedrine sulfate was used in doses of three tablets in the morning. The patient is definitely brighter, shows much more energy and has less tendency to retreat, and his answers are not so fragmentary. There are, however, no heterosexual activity and no urge to enter into industrial life. The personality seems "pushed forward," and his mental life seems more coherent and integrated, although there is by no means real recovery from the condition.

CASE 4.—M. D. has been under my care for about six years. One of his brothers had a manic-depressive psychosis, and another brother had hypertensive heart disease. The patient has always been of a morose, rather penurious, shut-in type. Six years ago, during a business crisis, he passed into a state of profound depression which reached the depressive state of manic-depressive psychosis, with somatic delusions, a marked sense of guilt and unworthiness, a sense of impending disaster, agitation and a variety of visceral disturbances, such as loss of appetite, disturbance of sleep and failure of the sexual function. He recovered from the acute phases of this condition after about a year of illness, but since that time he has remained in what may be called a neurotic phase. He continually complains of pain, weakness, disturbance in sleep and in the appetite, paresthesias throughout the body and lowered desire and satisfaction of all types. He has never been able to concentrate so as to go back to work. The main mood has been a combination of fear, depression and fatigue.

During all this time various methods of treatment have been followed. About the only relief that he obtained was during short residences in a sanatorium in which the prevailing treatment was a combination of dietary regulation and physical therapeutics. No drug had any effect on his mood. Caffeine, strychnine, sedatives, thyroid, extract of adrenal gland and many other preparations were used, without result.

Six weeks ago the use of benzedrine sulfate was started as a regular treatment, the dose being 20 mg. in the morning and 10 mg. at noon. This treatment has been the only one which has had any effect on the patient's sense of well-being. He stated that he has felt better during this period than at any other time. He has been more cheerful; there has been less complaint; he has shown some desire to go back to his business, and those in immediate contact with him report that he is "easier to live with."

It cannot be stated that he has in any fundamental sense recovered. If the use of the drug is discontinued for a few days he falls back into his previous mood. He is unable, even when he is taking the preparation, to carry on activities in a normal fashion. He has to guard his output of energy and avoid the strains and stresses of life. However, an ameliorative influence is definitely demonstrable,

and since the background of his condition has been so constantly adverse it can safely be assumed that it is the treatment and not coincidence which is responsible for the beneficial results.

CASE 5.—A. M., a man aged 64, a minister, passed from a state of repeated attacks of depression with self-accusation and retrospective delusion formation into a chronic state in which the fear that he had contracted syphilis in his youth and that he had sinned on various occasions and these misdoings were known to his community dominated his whole life, disturbing his sleep, appetite and energy and creating melancholia. He made no progress during the past year until about two months ago, when he was given 20 mg. of benzedrine sulfate on arising and at 11 a. m. There was in no fundamental sense recovery, but he stated that the mornings have become much more pleasant and that he is less obsessed with fear during this period of the day. In the afternoon the fears return, and he is agitated, but not more so than prior to the treatment.

The amelioration of the symptoms was so important to him that he asked to take the medicament throughout the day, but experience showed that in his case taking it throughout the day destroyed his sleep and rendered him tremulous. With 20 mg. a day there was considerable improvement; with larger doses his welfare was affected.

CASE 6.—L. T., a man aged 29, has a long history of sexual maladjustment. He seems to have a facility for falling in love with the wrong woman, and his affairs end after a hectic beginning with a long period in which he is gradually excluded from the emotional scene. Following the latest affair, which had lasted about two years, he became depressed and complained of marked paresthesias and then began to become panicky when he left home. There was marked hypochondriasis, apparently on the basis of the paresthesias which he experienced, which culminated in the fear that he was becoming insane.

This patient was given benzedrine sulfate immediately, without any other medication. Whether the result was coincidental or therapeutic, improvement was immediate. The fear gradually disappeared, and he is now on the way to recovery from this particular attack. In this instance the emotional state seemed to improve rapidly, and the fear disappeared with unusual celerity.

CASE 7.—G. R., a man aged 22, of marked conscientiousness of the overscrupulous type, worked very hard and maintained a repressed sexual and social existence. He became depressed, anxious and sleepless, lost his appetite and the sense of energy and acquired the idea that persons were talking about him. However, this seemed to be not so much an expression of hostility as one of self-depreciation. This is an important differentiation, since the delusion of persecution has, on the whole, a different prognostic significance than the delusion of unworthiness. There was some degree of insight in that he was sure some of the time that his "ideas" were only imaginary, but at the height of an emotional response he lost insight.

A certain amount of psychotherapy was carried out, as in all these cases. The situation was made reasonably clear and a change of life advocated. He made a thorough change in his relationships to others, and, whether owing to this or to the effect of the drug, his mood became definitely altered. He stated, however, that the feeling of depression, fatigue and unworthiness that he had in the morning lifted within an hour after the ingestion of the 20 mg. of the preparation, so it is probable that there was some relationship between the change in his attitude and the change produced in his mood. At any rate, improvement has continued, although he is by no means well.

Cases like those just cited could be easily multiplied from the experience of the past six months. Cases in which the patient seemed to be suffering from the same general condition yet showed no improvement during the same treatment can also be cited. As one of the companion papers [2] shows, benzedrine sulfate has a marked effect on the tone of the gastro-intestinal tract. Our cases have not been adequately studied in relationship to this, and it is probable that the state of tonus of the gastro-intestinal tract plus the prevailing cardio-arterial condition should be taken into account before benzedrine sulfate is administered.

There were two cases in which the effects were adverse which are important.

CASE 8.—L. F., a man aged 53, a bank teller, experienced within the past year a sense of guilt in respect to previous transactions (retrospective delusions of sin) and subsequently the belief that he was being spied on, that persons knew about his past falsification and that he would some day be arrested and punished for it. The patient was clear so far as his intelligence was concerned and had a certain amount of insight in that he realized, after the situation was explained to him, that it was his depressed state of emotion which was the basis for the delusions.

A few days after the administration of benzedrine sulfate he became excited, noisy and threatening, and his wife telephoned in great alarm from a camp in Maine, where he was staying, that he had become almost uncontrollable, whereas up to this time he had been well behaved, quiet and orderly and at no time had shown signs of excitement or violence. With the discontinuance of the use of the drug the excitement subsided, and he remained quiet from that time on.

CASE 9.—G. E., a man aged 25, at the age of 16 experienced headache, a deep sense of inferiority, a feeling that he could not look persons in the eye and a depressed mood. This was followed by complete retreat from the society of others and from activity. At the age of 18 he was sent to a state hospital, where he remained for four years; there the condition was diagnosed as dementia praecox. I do not agree with this diagnosis. He came under my care three years ago with the proposal that he allow himself to be experimented on in order to discover, if possible, a cure for his condition. He has been treated by practically every physiologic and pharmaceutic method possible. In a neighboring institute for persons with neuro-endocrine disorders a diagnosis of pituitary and thyroid deficiency had been made, although the grounds for this do not seem clear. He was given all manner of endocrine products, without the slightest result so far as change was concerned. His statement after each series of treatment was to the effect that he felt worse, his head was more confused and he could not think, despite the fact that his speech at all times remained coherent and his answers relevant, with no evidence of retardation or splitting of thought. At one time he was treated for a month by sedation to the point of stupor, without the slightest benefit. Probably every preparation of the anterior and of the posterior lobe of the pituitary gland was used for periods sufficient to produce results, and even insulin was used, in doses of 10 units given twice a day, without any change in his conduct or in his subjective reactions.

A month ago the use of benzedrine sulfate was started. At first the patient stated that he felt more energetic. However, the point was reached where the family complained that he became quarrelsome and disagreeable, even threatening.

---

2. Myerson, A., and Ritvo, M.: Benzedrine Sulfate and Its Value in Spasm of the Gastro-Intestinal Tract, J. A. M. A. **107**:24 (July 4) 1936.

There was an alteration in personality, which he explained as follows: Previously he tended to hide his hostile feelings, but under the influence of the preparation he no longer cared to hide them and showed what he really felt. The change in conduct, however, was sufficiently alarming to preclude any further use of benzedrine.

It may be stated at this point that the eighteen patients suffering from dementia praecox whom we treated for a considerable period with this drug showed no important deviation from their prevailing mood and attitudes. Thus the drug, had no effect in catatonic states and none, so far as we could see, in hebephrenia.

SUMMARY AND CONCLUSIONS

A systemic study of the effects of benzedrine sulfate on mood and fatigue has not been made. Certain effects, however, may be stated to exist:

First, normal nonpsychotic and nonneurotic persons who suffer from the fatigue and slight malaise due to insufficient rest, especially to insufficient sleep, receive immediate benefit and relief of a pleasant type when from 5 to 20 mg. of benzedrine sulfate is taken on arising. When this dose is taken toward the latter part of the day sleep is impaired in a striking manner. Thus, as an emergency measure the drug is probably of decided benefit.

Second, in certain cases of the neuroses associated with depression, fatigue and anhedonia and in certain cases of the minor stages of the psychoses of the same general type, benzedrine sulfate acts as an ameliorative influence. It is not in any sense curative and its effects are not permanent, but it helps to dissipate the morning apathy and depression, and its ameliorative effect is sufficiently important to recommend it during the treatment of the patient by other means and while the process of natural recovery is taking place.

Since this paper was written an article by Peoples and Guttmann, "Hypertension Produced with Benzedrine," has appeared in the Lancet (**1**:1107 [May 16] 1936).

News and Comment

ORGANIZATION OF THE AMERICAN LEAGUE AGAINST EPILEPSY

The members of the International League Against Epilepsy who are resident in the United States or Canada have organized themselves into an American branch of the League. A constitution has been adopted and officers have been elected, as follows: president, William G. Lennox, M.D., Boston; first vice president, Mynie G. Peterman, M.D., Milwaukee; second vice president, Temple Fay, M.D., Philadelphia; secretary-treasurer, Frederic A. Gibbs, M.D., Boston, and vice president of the International League for America, Walter B. Cannon, M.D., Cambridge, Mass.

The chief qualification for membership is an active interest in the problem of epilepsy or in the care and treatment of persons with epilepsy. Persons who are not physicians may be admitted up to 10 per cent of the membership. Dues, which include membership in the International League, are $3.75 for four years. The next annual meeting of the League will be at the time of the Annual Session of the American Medical Association. Persons desiring to join should communicate with the Secretary, Dr. Frederic A. Gibbs, 910 Medical Building, Boston City Hospital, Boston.

INTERNSHIPS AND RESIDENCIES IN PSYCHIATRY

The Psychiatric Division of Bellevue Hospital announces that applications will be received for appointment as intern or resident in psychiatry. There are ten internships for a period of one year, paying $15 a month, with maintenance. Five appointments are made January 1 and five July 1. These appointments are made through the New York University Medical College. There are also four residencies in psychiatry for a period of one year, paying $50 per month. Two appointments are made January 1 and two July 1.

Graduates of a class A medical school who have completed one year of general hospital internship are eligible for appointment as interns. Graduates of a class A medical school with one year of general hospital work and one year of psychiatric work in an approved psychiatric hospital are eligible for appointment as residents.

Applications for internships and residencies should be made to Dr. Karl M. Bowman, Director, the Psychiatric Division of Bellevue Hospital, New York.

Abstracts from Current Literature

Anatomy and Embryology

THE PRESENCE OF SENSORY NERVE CELLS IN THE CENTRAL ROOT OF THE TRIGEMINAL NERVE. GUSTAVUS A. PETERS, J. Comp. Neurol. **62**:349 (Oct.) 1935.

This paper is concerned with an explanation of the restoration of sensation after subtotal section of the central root of the trigeminal nerve. Four central roots of the trigeminal nerve were obtained from the dog, rabbit, guinea-pig and ox, six central roots from the pig and fourteen central roots from the cat. These tissues were fixed immediately in a dilute solution of formaldehyde U. S. P. (1:10). Twenty central roots of the nerve of man were also available. All the roots were embedded in paraffin, and serial transverse sections were made. In counting nerve cells only those showing a definite nucleus and nucleolus were used. Cells were observed in the central roots of all the animal forms. The number varied not only in different animals but on opposite sides of the same animal. The diameters of the cells varied from 12 to 90 microns. The occurrence was irregular from the pons to the semilunar ganglion. Cells were slightly more frequent in the motor than in the sensory roots. They were located between the fibers of each root, between the roots themselves and beneath the pia. With few exceptions the nerve cells in the central roots exhibited most of the characteristics of the sensory type. In one root of the human nerve, an additional ganglion was observed within 2 mm. of the semilunar ganglion on each side, but not connected with it. Peters believes that the presence of sensory nerve cells in the central root of the fifth nerve proximal to the point of surgical section provides an adequate explanation for the return of sensation reported in cases in which operation is performed for the relief of trigeminal neuralgia. He suggests severing the central root at the pons to prevent return of sensation.

ADDISON, Philadelphia.

THE DEVELOPMENT OF THE CEREBELLUM IN THE BAT (CORYNORHINUS SP.) AND CERTAIN OTHER MAMMALS. O. LARSELL and R. S. DOW, J. Comp. Neurol. **62**:443 (Oct.) 1935.

The brains of fetal and adult bats, fetal and adult rats and fetal, young and adult moles were available for this study of the cerebellum. A gross study of the lobes and fissures was made, and blotting-paper models were reconstructed.

The cerebellum of the bat, mole and rat shows in its development two fundamental divisions of bilateral origin, namely, the corpus cerebelli and the flocculonodular (auricular) lobe. Except for relative size, they correspond to the corpus cerebelli and the auricular lobe of the lower vertebrates in development and relationship. In the early stages the flocculonodular lobe is relatively large, but it becomes overshadowed by the corpus cerebelli in the course of development. The corpus cerebelli, as it increases in size, shows marked foliation of its cortical portion. On the grounds of the comparative anatomic structure and the connections of root fibers and fiber tracts in these mammals, Larsell and Dow regard the flocculonodular lobe as the primary cerebellar projection zone for vestibular impulses and the corpus cerebelli as the corresponding zone for impulses of muscle sense.

ADDISON, Philadelphia.

MORPHOLOGICAL AND FUNCTIONAL DEVELOPMENT OF THE MEMBRANOUS LABYRINTH IN THE OPOSSUM. O. LARSELL, E. MCCRADY JR. and A. A. ZIMMERMANN, J. Comp. Neurol. **63**:95 (Dec.) 1935.

The vestibular mechanism of the opossum does not begin to function until forty-one days after birth, yet at birth the animal displays independent migration to its mother's pouch. Negative geotropism is the guiding factor in this act. In this study the embryologic development and histogenesis of the membranous labyrinth and its nerves are traced from the earliest embryologic primordia through the entire period of occupation of the pouch. The animal is born late in the thirteenth day of fetal life and remains in the pouch for about fifty days.

Sixty-three series of sections of embryos from the eight somite (medullary plate) stage to birth and sections of the heads of pouch young opossums of nine sizes were studied. From twenty-nine days after birth onward, a series of tests for vestibular reflexes were performed, and one specimen of each stage was treated with a modification of Ramón y Cajal's reduced silver method to stain nerve endings in the membranous labyrinth. Auditory tests were also made. In the early part of the ninth day of development the otic placode and the anlage of the acousticofacial ganglionic complex are recognized. By the middle of the ninth day the otic placode has become a deep cup. The endolymphatic duct is seen during the later part of the tenth day. Nerve terminations were seen in relation to both vestibular and cochlear hair cells long before there was any indication of functional response to stimuli for either the vestibular or the cochlear apparatus.

Acoustic reflexes appeared at fifty days after birth, first to high, shrill notes and on subsequent days to successively lower notes in the musical scale. The differentiation of the organ of Corti was from the basal coil toward the helicotrema. The authors suggest that the development of myelin on the preexistent nerve fibers may be a result of the activity of these fibers induced by the capacity of the end-organ to produce a nerve impulse.

ADDISON, Philadelphia.

NEUROFIBRILLAR DEVELOPMENT OF CAT EMBRYOS: EXTENT OF DEVELOPMENT IN THE TELENCEPHALON AND DIENCEPHALON UP TO 15 MM. WILLIAM F. WINDLE, J. Comp. Neurol. **63**:139 (Dec.) 1935.

Embryos of from 13 to 15 mm. in crown-rump length exhibit some of the first responses to adequate forms of mechanical and faradic stimulation. The development of the forebrain is described in relation to the unfolding of systems of fibers in embryos up to 15 mm. in length. Fourteen embryos from 5.5 to 15 mm. treated with the pyridine-silver method were used. Many of these stages were tested physiologically, and the responses have already been described.

The first neuroblasts of the forebrain to show neurofibrils with the method used appeared in the ventrolateral wall of the neural tube of the 5.5 mm. embryo, at the junction of the diencephalon and the telencephalon. They form a group which is the anlage of the motor portions of the tegmentum and subthalamus. The axons of the latter center all course caudad, without crossing the floor plate. This is the rostral component of the medial longitudinal fascicle. The second group of neuroblasts Windle describes as the supra-optic system, first seen in the embryo of 6 mm. The third system is olfactory and was observed in an embryo at 7 mm. At 11.5 mm. there are three main bundles of fibers present in the primitive rhinencephalon. The most ventral is designated as the olfactohypothalamic tract, the most dorsal the olfactosubthalamic tract and the lateral the lateral olfactory tract. Most of the structures appearing ventral and rostral to the hypothalamic sulcus before the 13 mm. stage seem to be concerned with the olfactory and optic systems. Nerve fibers from more caudal parts of the brain grow forward into the diencephalon to end in the anlage of the thalamus. The fibers appearing first, at 8 mm., have been designated the lemniscus system. Thalamostriatal and thalamocortical neurons begin to form at the 11.5 mm. stage but none has reached the cortex at the 15 mm. stage. In view of the immature state of the centers of the forebrain,

Windle concludes that, if integrating mechanisms are functional in the embryo, they must be looked for in parts of the brain below the diencephalon.

ADDISON, Philadelphia.

THE FIRST NEUROFIBRILLAR DEVELOPMENT IN ALBINO RAT EMBRYOS. WILLIAM F. WINDLE and RAYMOND E. BAXTER, J. Comp. Neurol. **63**:173 (Feb.) 1936.

One litter of seven embryos of the albino rat, two hundred and seventy-two hours after insemination, exhibited considerable variation in the degree of development of neurofibrils. The embryos, 3 to 4 mm. in length, shrank 50 per cent in the fixing fluid. A modification of the pyridine-silver reduction technic was used. The state of development of neuroblasts in this litter varied directly with the size of the specimen. In the smallest embryo the only neuroblasts showing neurofibrils were seen in the rhombencephalon. The trigeminal motor nucleus, the facial motor nucleus and the glossopharyngeal-vagus-accessory nucleus were present. Although the largest embryo after fixation was not even 0.6 mm. longer than the smallest, Windle and Baxter describe an appreciable increase in the neurofibrillar development. All the visceral motor nuclei in the first embryo were larger, contained more cells and sent more axons into the motor roots than the corresponding nuclei in any of the other embryos. Nuclei of the oculomotor, trochlear, hypoglossal and upper spinal nerves were present. Sympathetic nerve cells were seen along the foregut. Sensory cells were seen in the trigeminal, acousticofacial and glossopharyngeal-vagus ganglionic anlagen. No neuroblasts of the brain or spinal cord of any embryos in this series had progressed beyond the unipolar stage.

Neurofibrils begin to form in the cytoplasm of cells while they are still attached to the internal and external limiting membranes of the neural tube. Four stages in the development of the neuroblast are described as seen in these embryos: prefibrillar, spindle-shaped apolar, primitive bipolar and unipolar nerve cells. On the basis of these observations Windle and Baxter believe that there is no morphologic evidence for Bok's hypothesis of stimulogenous fibrillation.

ADDISON, Philadelphia.

DEVELOPMENT OF REFLEX MECHANISMS IN THE SPINAL CORD OF ALBINO RAT EMBRYOS: CORRELATIONS BETWEEN STRUCTURE AND FUNCTION, AND COMPARISONS WITH THE CAT AND THE CHICK. WILLIAM F. WINDLE and RAYMOND E. BAXTER, J. Comp. Neurol. **63**:189 (Feb.) 1936.

Many of the embryos of the rat described in this paper were tested physiologically for behavior reactions and later were treated with the silver-pyridine technic. Ten embryos from several litters from three hundred and seventy-four to three hundred and seventy-eight hours after insemination were studied. Five gave no response to stimulation, and five exhibited reflexes of the forelimb. The first neuroblasts to differentiate in the spinal cord were seen in the motor column of embryos 4 mm. in length. The neuroblasts of the spinal ganglia appear later than those of the motor column, and the dorsal funiculus is seen at the 7 mm. stage. Both commissural and association elements are present at this stage. Between the 9 and the 11 mm. stage the spinal cord increases in size rapidly. The columns of motor neuroblasts form two distinct columns, for trunk and for limb. The increase in the number and length of sensory collateral fibers in the brachial spinal segments is correlated with the appearance of certain induced behavior responses of the embryo, which have the characteristics of simple spinal reflexes. This is the third species of animal that Windle has studied in which he reports that the appearance of collateral branches of primary afferent neurons is correlated with the appearance of elicited responses of the anterior extremity. The chick and cat have been reported on previously. He believes in the segmental character of the early behavior manifestations, for he can explain, on the basis of the structures of the spinal cord in the 16½ day old embryo of the rat, all movements of the forelimb which he was able to induce at that stage.

ADDISON, Philadelphia.

DOMINANCE OF HYDRANTHS INDUCED BY GRAFTS IN CORYMORPHA. C. M. CHILD, J. Exper. Zoöl. **71**:375 (Oct. 5) 1935.

In a further study of the physiologic effects on the host stem of lateral hydranths induced by grafts of stem pieces, three series of experiments were performed on the tubularian hydroid Corymorpha palma, in which small stem pieces were implanted into the entodermal parenchyma of from 40 to 50 mm. hosts through lateral incisions. In the first series the host hydranth was removed at the time of operation. In the second series one half of the proximal part of a twenty-four hour hydranth primordium was used for grafts. In the third series the host hydranth was not removed, but on the second day after implantation the host stem was cut from 5 to 6 mm. distally and proximally to the induced hydranth. It was found that a varying degree of inhibition and altered polarity in the development of the host hydranth was effected by the induced hydranth. It was concluded, therefore, that the induced hydranth acts as an organizer in determining the reorganization of the host piece.

WYMAN, Boston.

AN EXPERIMENTAL STUDY OF THE ORIGIN OF PIGMENT CELLS IN AMPHIBIA. GRAHAM P. DUSHANE, J. Exper. Zoöl. **72**:1 (Nov. 5) 1935.

In an extensive study to test the hypothesis for the origin of melanophores from connective tissue, the results led to a confirmation of the theory of derivation from the neural crest. Homoplastic and heteroplastic transplantation and explantation of pieces of the ganglion crest from the trunk region, the nerve cord, dorsal and flank ectoderm and mesoderm were performed on embryos of Amblystoma punctatum (Linnaeus), Amblystoma tigrinum (Green) and Amblystoma mexicanum (both black and white axolotls). The methods were those in general use, but rigid sterile precautions were taken in all operative procedures.

Evidence was obtained that melanophores invariably develop in explanted or transplanted neural folds, that in flank ectoderm and mesoderm this ability is not acquired until much later, that no melanophores appear in the trunk region of embryos deprived of the neural folds and that melanophores of the donor type arise from homoplastic or heteroplastic transplants of ectoderm and neural crest and then migrate under the host ectoderm. It appears definitely proved, therefore, that dermal melanophores arise from the ganglion crest. It was impossible to determine decisively, however, whether the epidermal melanophores were derived from the cells of the neural crest or were induced from epidermal cells by the neural crest. The evidence also indicated that the neural crest is the source of the dermal lipophores.

The evidence showed that the primordial melanophores migrate to their definitive positions before acquiring pigment. In the white axolotl the dependent dermal melanophores developed melanin only in the presence of transplanted pigmented epidermis. They differ, therefore, from the normal melanophores of the white axolotl, which form pigment independently of the epidermis.

WYMAN, Boston.

HETEROPLASTIC TRANSPLANTATION OF THE HYPOPHYSIS IN AMBLYSTOMA. H. BYTINSKI-SALZ, J. Exper. Zoöl. **72**:51 (Nov. 5) 1935.

As an approach to the question whether the hypophysis of a neotenous species exerts any influence on the behavior of a species that normally metamorphoses, and vice versa, the epithelial anlage of the hypophysis (pars buccalis) of the neotenous Amblystoma mexicanum and that of the metamorphosing Amblystoma tigrinum were exchanged in the early tail-bud stages. The grafts were placed in their normal positions. The mortality rate was high for the groups in which experimental operation was performed (twenty survivors in one hundred and ninety subjects), but all the sixteen animals used as controls survived. In six instances in which A. tigrinum received heteroplastic transplants taken from A. mexicanum, growth and metamorphosis were normal. In the remaining twelve instances

development and body color were normal up to from ninety-seven to one hundred and sixty days, when the animals suddenly became whitish, and metamorphosis failed to occur. This was due to resorption of the graft, and increasing incompatibility of the tissues of the two species was demonstrated with increasing age. Histologic study of the infundibular walls showed that in these instances the graft while viable induced normal development. Decisive results were obtained in two instances in the series in which A. mexicanum was implanted with grafts from A. tigrinum. Development was normal, and metamorphosis failed to occur up to and after three hundred and seventy-five days.

The results indicate that in the hypophysis-thyroid mechanism for metamorphosis the pituitary does not act independently. The connections between the hypophysis and the thyroid are not quantitatively fixed but are probably controlled by another factor within the host.

WYMAN, Boston.

EXPERIMENTAL RESEARCHES ON THE ORIGIN OF THE ACOUSTIC GANGLION IN AMPHIBIAN EMBRYOS. ERNEST VAN CAMPENHOUT, J. Exper. Zoöl. **72**:175 (Nov. 5) 1935.

In the amphibians Rana pipiens and Amblystoma jeffersonianum, unilateral extirpation of the otic placode, unilateral extirpation of the neural crest of the hyoid arch, extirpation of the rhombencephalon with the neural crest or heterotopic transplantation of the placode were performed on embryos from the stage of the wide-open neural fold (Amblystoma) to the stage of the beginning tail bud (frog).

The following results were obtained: absence of the acoustic ganglion after extirpation of the otic placode; presence of a normal ear with normal acoustic ganglion and nerve after extirpation of the neural crest; formation of an acoustic ganglion without the acoustic nerve after removal of the rhombencephalon and adjacent neural crest; migration of acoustic ganglion cells from the otic epithelium, and formation of the ear vesicle with acoustic ganglia from heterotopic grafts.

These observations in amphibians were in complete accord with the results of previous work on the development of the acoustic ganglion in pig embryos. Since the work demonstrates that in two widely separated groups, amphibians and mammals, the acoustic ganglion cells are derived from the otic epithelium, without contribution from the neural crest, it is suggested that this origin of the acoustic ganglion is the same for the entire vertebrate series.

WYMAN, Boston.

THE CORTICAL TASTE AREA. ALEXANDRA ADLER, Ztschr. f. d. ges. Neurol. u. Psychiat. **152**:25, 1935.

An unusual case is reported in which, in addition to neurologic symptoms, there was unilateral disturbance of taste without any other sensory manifestations. A meningioma over the site of the first temporal gyrus and involving the island of Reil was completely extirpated, resulting in a return of the sense of taste. A theoretical discussion is given of the relationship of this area to the elaboration of the sense of taste from a lower to a higher level. Although tracts for general and gustatory sensation do not travel from the thalamus to the cortex by a common path, nevertheless the cortical area of taste is connected with the cortical area of general bodily sensation.

MICHAELS, Boston.

SECRETORY FUNCTION OF THE DIENCEPHALON IN MAN AND ANIMALS. R. GAUPP JR. and E. SCHARRER, Ztschr. f. d. ges. Neurol. u. Psychiat. **153**:327 (Aug.) 1935.

Further histologic work has confirmed the previous studies of Gaupp and Scharrer that the nerve cells in some of the hypothalamic nuclei have secretory functions and that colloid bodies demonstrable in the tissue spaces of such nuclei are secretory products. Abel, Collin and Drouet and others have shown that

tissue extracts of the hypothalamus when injected into animals produce the same physiologic changes as hypophyseal substance (rise of blood pressure and expansion of melanophores). This result led these investigators, especially Collin, to conclude that the hypophyseal secretion passes up into the hypothalamic region. Gaupp and Scharrer deny the contention of some authors that the so-called colloid secretory products are pathologic. Their strongest argument is that identical structures have been observed in these same cell groups in a wide variety of animals, including invertebrates. It is hardly conceivable that all these animals were fortuitously afflicted by the same malady in the same part of the brain. Such a conception does not agree with what is known of comparative pathologic changes. Gaupp and Scharrer believe that the cells of the nucleus supra-opticus and nucleus paraventricularis have secretory properties. In 1933 they observed colloid droplets in the cells of these hypothalamic nuclei in a girl who died of carbon monoxide poisoning. These structures resembled closely homologous changes noted in reptiles and amphibians by one of the authors. This stimulated further investigation of the vegetative nuclei in the human brain to corroborate the hypothesis of the existence of a hypothalamic-neuro-endocrine system. Thirty-five human brains were examined.

The cell structure of the nucleus supra-opticus and nucleus paraventricularis is similar. The rich vascularity of these nuclei has been commented on by many investigators. Even endocellular capillaries have often been seen. The cells are often lined up near large blood vessels. Formation of vacuoles, especially in the periphery, is characteristic of these ganglion cells. The shape of the cell differs with the position of the nucleus, being more fusiform when it is surrounded by more nerve fibers. Cells with two nuclei are common, one in almost every two cells studied. These multinucleate cells usually contain more tigroid substance than cells with one nucleus. The cytoplasm is more homogeneous, and they contain fewer vacuoles. These facts suggest that they are younger cells. The authors noted amitosis in these cell groups, even in the postfetal period. Multinucleate cells are less frequent in the homologous groups in lower animals. The most characteristic feature of all these cells is the deposit of a colloid substance, which is demonstrated most clearly by the Van Gieson technic. It appears at first as fuchsinophilic granules among the tigroid granules near the periphery of the cell. As the amount of colloid increases the Nissl substance diminishes. Free colloid is occasionally observed outside the cells, especially near the blood vessels. Similar changes were noted in the hypothalamic nuclei in mammals, reptiles, fishes and even invertebrates.

The striking similarity of these nuclei in man and lower animals is not a coincidence. It has been shown that hypothalamic tissue extracts are more efficacious in animals that have been hypophysectomized. The effect of the hypothalamic centers does not depend wholly on neurogenic control but is mediated also through the elaboration of substances which are poured into the blood stream. They exert hormonal control through the regulation of hypophyseal function and by the secretory properties of their cells.

SAVITSKY, New York.

Physiology and Biochemistry

THE VISCEROGALVANIC REACTION. E. A. SPIEGEL and M. G. WOHL, Arch. Int. Med. **56**:327 (Aug.) 1935.

In visceral disease segments of the spinal cord corresponding to the organ involved are in a state of hyperexcitation. To localize this objectively, Spiegel and Wohl employed a technic to measure the electric potentials of the dermatomes. A galvanometric potentiometer was used, and the potentials led off from the areas were measured in millivolts. Thirty-two patients with pain in the trunk comprised the subjects of the experiment, and fifteen persons without visceral disease constituted the controls. Among the latter the highest values in the dermatomes of the trunk never exceeded 31 millivolts. On the other hand, all but three of the group with pain in the trunk showed some abnormality of electric potential. For ten of the twenty-five patients with areas of abdominal or thoracic hyperalgesia, potentials in

excess of 31 millivolts were recorded; for thirteen of the twenty-five, the potentials of the hyperalgesic zones exceeded the maximal potentials on other parts of the trunk by more than 10 millivolts. For some of the patients suffering from visceral disease without pain in the trunk, high potentials were recorded. In one instance a patient with coronary thrombosis who was kept free from pain by morphine displayed a high potential in the left side of the chest without having any hyperalgesia. This would suggest that the viscerogalvanic reflex is independent of higher brain centers. Nor was any relation found between the reflex and the skin temperature or between the viscerogalvanic response and the visceropilomotor reflex. A close correspondence between the viscerogalvanic reaction and the activity of the sweat glands could be inferred, although direct proof was not available.

The viscerogalvanic response here described must be distinguished from Tarchanoff's phenomenon. The latter is an alteration in galvanic skin response following psychic excitation and differs from the viscerogalvanic response in affecting the whole surface of the body rather than merely body segments. Since the visceral disease process which brings about the viscerogalvanic reaction is a more or less continuous process, this reaction also differs from the Tarchanoff phenomenon in being more sustained.

DAVIDSON, Newark, N. J.

THE INFLUENCE OF ADDITIONAL PITUITARY ANLAGEN UPON THE CIRCULATORY SYSTEM OF THE DEVELOPING URODELE: A CONDITION PARALLELING HYPERTENSION IN THE MAMMAL. RAYMOND F. BLOUNT, J. Exper. Zoöl. **71**:421 (Oct. 5) 1935.

In Amblystoma punctatum two additional pituitary anlagen were implanted during the embryonal period. The development of the circulatory system under the influence of the experimentally produced excess of hormone was observed and checked by observations on numerous controls and on the hypophysectomized donors. This modification of the hormonal balance produced a condition which represented a truly hypertensive state.

Observations on the developing vascularity of the gills, caudal fins and limbs showed that the size and number of the capillaries formed was reduced to about one-half those of the normal controls. Correlated with this diminution in vascularity and increase in peripheral resistance were an obvious increase in blood pressure and a reduction in the size of the integumentary peripheral parts. Owing to the contraction of the vascular elements the size of the spleen was less than 50 per cent that of the normal. Marked dilatation or hypertrophy of the heart or both occurred; on the basis of pericardial measurements there was a relative increase in length of 14 per cent and in width of 35 per cent. Volume determinations showed hypertrophy of the ventricular wall of from 126 to 412 per cent. Passive congestion of the liver and renal glomeruli characteristic of those observed in hypertension were noted.

Blount states that this is the first work which definitely indicates a correlating mechanism linking the posterior pituitary secretion with hypertension.

WYMAN, Boston.

FACILITATION AND INHIBITION IN THE SUPERIOR CERVICAL GANGLION. J. C. ECCLES, J. Physiol. **85**:207 (Oct. 26) 1935.

Since Langley's classic investigations, the sympathetic ganglion has been regarded merely as a relay station in the peripheral sympathetic pathway, each preganglionic fiber being in sole functional connection with a group of ganglion cells. In Eccles' previous paper the last mentioned view was shown to be incorrect, for many ganglion cells are excited by each of two groups of preganglionic fibers. This overlapping distribution of preganglionic fibers on ganglion cells brings with it potentialities for coordination, each postganglionic neuron forming a final common path for the various preganglionic fibers in functional connection with it. This paper investigates these possibilities.

Eccles found that besides producing a discharge of impulses from some ganglion cells, a submaximal preganglionic volley sets up in both these and other ganglion cells an excitatory condition which increases the response to a subsequent submaximal volley (spatial facilitation of the subliminal fringe) and shortens its synaptic delay (temporal facilitation). With S_1 ganglion cells this facilitating effect persists for about 150 microseconds, but with S_2 ganglion cells it is less in extent and duration, presumably on account of the simultaneous presence of inhibition. Facilitation is also observed after a maximal volley or between volleys in different groups of preganglionic fibers. Spatial facilitation usually undergoes a relative increase as the preganglionic volleys become smaller, and facilitated responses occur even when each volley alone is subliminal, indicating that a single preganglionic impulse fails to set up a discharge from any ganglion cell.

The facilitating effect of a variable first preganglionic volley or a second volley becomes greater as the size of the first volley increases to that of the second but is usually not altered by further increase of the first volley, a result suggesting that the central excitatory state of a ganglion cell is diminished when the ganglion cell discharges an impulse. Facilitation is unaffected by physostigmine or anesthetics but is abolished by doses of nicotine too small to affect the transmission of impulses through the ganglion.

In addition to this facilitating effect, a preganglionic volley also has an inhibitory action, largely confined to S_2 ganglion cells, which reaches its maximum in about 150 microseconds and completely passes off at about 600 microseconds. Within limits this inhibition increases both absolutely and relatively as the second (inhibited) volley is made smaller, showing that the less the excitation of a ganglion cell the more easily it is inhibited. The preganglionic fibers which inhibit and those which excite S_2 ganglion cells have identical thresholds.

Two inhibiting volleys with a short interval have a greater inhibitory effect than either alone, though there is considerable occlusion if the volleys are large. However, if the second volley is at a longer interval after the first, there is diminution of the first inhibitory effect for as long as 150 microseconds, an effect probably attributable to the reaction of the ganglion cells to the inhibition of the first volley, whereby the opposing excitation of the second volley is increased and prolonged and its inhibition decreased.

Doses of nicotine too small to prevent transmission of impulses may prevent an inhibitory effect from being produced. Still smaller doses of nicotine serve for analysis of the overlapping excitatory and inhibitory effects set up by a preganglionic volley, for the inhibitory effect then set up in the absence of complicating facilitation is at a maximum at least as soon as the end of the refractory period. This suggests that the normal phase of increasing inhibition is really due to the more rapid decrease of the opposing facilitation.

These excitatory and inhibitory states of ganglion cells resemble the corresponding states (central excitatory and central inhibitory states) of the spinal cord and show that the superior cervical ganglion must be regarded as a coordinating center as well as a transmitting and distributing station. ALPERS, Philadelphia

ON THE ALLEGED OCCURRENCE OF "KRAMPFSTOFFE" IN ACETONE EXTRACTS OF MAMMALIAN BRAIN. ERIC HOLMES, J. Physiol. **85**:400 (Nov. 22) 1935.

In a recent series of papers Kroll claimed that by making an acetone extract of the fresh brains of animals killed during convulsion material is obtained which produces convulsions when injected intravenously into other animals. The brains of sleeping animals, on the other hand, when similarly treated yield a sleep-producing substance, while the extract of the brains of normal animals has no effect.

Kroll's technic is simple. Convulsions are produced by electrical stimulation of the cerebral cortex, by the use of convulsant drugs or by inducing insulin hypoglycemia. Sleep is induced by hypnotic drugs, or the brains of hibernating animals are used. The animal is killed, and the brain is excised, rapidly ground

up with sand and extracted with acetone. The acetone is removed by distillation in vacuo at a low temperature, and the resulting aqueous suspension is diluted with physiologic solution of sodium chloride and injected intravenously into another animal.

Holmes found that extracts of rabbit's brain, made according to Kroll's directions, are lethal on intravenous injection because they cause stoppage of the heart. There is no evidence that they exert any direct effect on the central nervous system. The lethal effect is exactly the same no matter what may be the condition of the animal from which the brain is obtained. Kroll's statement that the extracts rapidly lose potency is not confirmed. The effect on the heart may be either mechanical or chemical. It has been found that the active portion of the preparation is the ether-soluble moiety of the solid matter. The turbid saline suspensions used might well be capable of causing emboli in the heart muscle. No gross evidence of this was obtained by subsequent perfusion of the hearts with a dye—the muscle substance was as evenly stained as that of the heart used as a control. On the other hand, a frog's heart, perfused by Clark's method, does not appear to be affected by the substance, and since the frog's heart has no coronary circulation this suggests that the effect on the mammalian heart was, in fact, due to embolism in some part of the coronary circulation.

ALPERS, Philadelphia.

CONTRIBUTION TO THE PHYSIOLOGIC ACTIVITY OF THE THALAMUS. D. NOICA and M. BALS, Encéphale **30**:554, 1935.

In a patient with parkinsonism, removal of the first two cervical sympathetic ganglia on the left side resulted in a condition similar to that following thalamic lesion. Nociceptive stimuli to the left side of the face were more disagreeable than those to the right and were perceived as a diffuse burning pain, becoming rapidly unbearable and persisting more than one hour after cessation of the stimulus. This sensation was accompanied by vasomotor disturbances in the same territory. These were most intense in the stimulated area. One year after the operation the vasomotor disturbances disappeared, but the hemihyperalgesia persisted. Three patients with epilepsy, who had undergone cervical sympathectomy on the left side, presented the same excessive nociceptive reactions on the left side of the face, but without the vasomotor disturbances. A patient with tabes in association with atrophy of the optic nerve failed to show any difference in the reactions of the two sides of the face after cervical sympathectomy on the right side. This apparent exception was explained by a general diminution of sensation in the face, which is considered proof that the trigeminus nerve was affected by the syphilitic meningitis and consequently could not transmit pain. These facts are in keeping with the experiments of Claude Bernard (1851) who found that after unilateral removal of the superior cervical sympathetic ganglion in the cat or the rabbit, sensation seemed intensified in the corresponding side of the face. Tournay (1931) obtained similar results in the paw of a dog after abdominal sympathectomy. Noica and Bals conclude that the sympathetic nervous system moderates the sensations resulting from nociceptive stimuli. The function is similar to that of the thalamus, as conceived by Head. While the cervical portion of the sympathetic system exercises this moderation only on the ipsilateral side of the face, the thalamus serves for the entire opposite side of the body.

LIBER, New York.

WRITING PRESSURE OF TWINS. MIGUEL CARMENA, Ztschr. f. d. ges. Neurol. u. Psychiat. **152**:19, 1935.

Twenty-nine pairs of identical (uniovular) twins and twenty-one pairs of nonidentical (biovular) twins were studied with reference to similarity in pressure while writing, which was recorded by a kymograph. The similarity was significantly more noticeable in the case of the identical twins, especially the males;

the females showed similarity, but it was not as great. The method of learning to write was the same for both sets of twins; the vocations were different for only seven pairs. The conclusion is drawn that hereditary predisposition plays an important part in the regulation and intensity of the movements and of the tonus of the muscles of the arms and hands (movements of an involuntary and automatic nature).

MICHAELS, Boston.

FURTHER STUDIES ON VITAMIN C IN THE BRAIN AND IN THE CEREBROSPINAL FLUID. F. PLAUT and M. BÜLOW, Ztschr. f. d. ges. Neurol. u. Psychiat. **152:** 84, 1935.

It was found that the vitamin C content of the brain in fetuses of rabbits and mice was much higher than in the mothers of these animals. In 43 human brains there was a decrease of the vitamin C content with an increase in age. In 125 specimens of spinal fluid the same tendency was observed. In 10 cases it was possible to determine the spinal fluid content during life and to compare it with the vitamin C content in the brain after death. There was a parallelism between the two. In comparison with other organs, the brain, next to the adrenal glands, has the highest content of vitamin C. In the brains of human fetuses, the vitamin C content is higher than in the brains of adults. In view of these observations, the question is raised whether vitamin C does not play a more important rôle in the function of the brain than in the function of organs with a lesser amount of this vitamin.

MICHAELS, Boston.

Psychiatry and Psychopathology

RORSCHACH'S INK-BLOT TEST AND RACIAL PSYCHOLOGY: MENTAL PECULIARITIES OF MOROCCANS. M. BLEULER and R. BLEULER, Character & Personality **4:**97 (Dec.) 1935.

Responses to the Rorschach test of a group of simple country folk from West Morocco, half of them Arabs and half Berbers, showed a marked preference for small detail. Small detail responses were even more frequent than among European patients with schizophrenia. A marked tendency was evident to combine detail according to the whim of imagination and not in accordance with any unifying principle, logical or affective. Good power of observation was indicated, but defective ability to think in a systematic, well organized way. In referring to an object, frequently a particular object was specified, e. g., "the horse on which you rode this morning." Their responses were influenced by inexperience in looking at pictures, but the question is raised whether this inexperience itself was not due to some racial peculiarity. The authors conclude that the traits revealed by the Rorschach test are in conformity with the characteristics of the Moroccans as shown in their national life, literature, art and science and that, accordingly, the test is a valuable tool with which to gage the character of a foreign people. They find in the Moroccan marked enthusiasm under the influence of momentary events and lively, extroverted interest in current episodes, but, in the long run and in the face of important problems of life, the attitude of a schizoid dreamer, self-centered, introverted, independent of the outer world and with a preference for seclusion.

MATHER, New Haven, Conn.

HOW THE MONTEFIORE SCHOOL PREVENTS CRIME. EDWARD H. STULLKEN, J. Crim. Law & Criminol. **26:**228, 1935.

The Montefiore School, Chicago, is one of two new special schools for truant and problem boys. It was opened in September 1929 and enrolls 510 boys, who are from 10 to 17 years of age. Classes do not average over 25 boys. The Chicago Board of Health furnishes the school with medical and dental services. A full time psychologist is assigned to the school by the Bureau of Child Study.

There is a special teacher of speech. Individual work is done with groups of boys having pronounced disability in reading and arithmetic, and all are given diagnostic tests to determine the difficulties. Attendance in the school has been over 89 per cent, in spite of the fact that 65 per cent of the boys were habitual truants before being sent there. Less than 18 per cent of the boys have had to be taken to the juvenile court. Approximately 500 boys have been saved from a court experience, and 350 boys have been saved from a parental school or institutional experience in the past five years. The school has attempted to create in its staff a mental hygiene point of view, in an effort to keep psychiatric principles an integrated part of the school system. Behavior difficulties among the children are carefully analyzed. The school curriculum is made more elastic, and difficulties in special subjects are corrected in order to enable a student to escape from a feeling of inferiority. The school tries to build up all conditions which tend to increase peace and satisfaction.

SELLING, Detroit.

INVESTIGATION INTO THE AFTER-HISTORY OF NINETY PATIENTS DISCHARGED FROM A MENTAL HOSPITAL AGAINST ADVICE. LOUIS MINSKI, J. Ment. Sc. **81**:509 (July) 1935.

The histories of ninety patients who left against advice a hospital for patients with mental disease were studied. Seventeen could not be traced; twenty-five were in hospitals for the treatment of mental disease; twenty-four had recovered; sixteen were at home, without showing improvement; seven had committed suicide, and one had died at home. Minski found that the largest group of patients removed against advice was composed of patients with depression whose conflict with the environment was not marked. In view of the large number of suicides, Minski believes that relatives should be urged to leave such patients in the hospital. The problem of the patient with depression is intensified by the fact that he usually comes back to a difficult domestic situation, which aggravates his illness. Relatives are usually more inclined to leave in the hospital the patients who are in a state of acute excitement.

KASANIN, Chicago.

CONTRIBUTION TO THE STUDY OF THE INVOLUTIONAL PSYCHOSES. G. HALBERSTADT, Ann. méd.-psychol. (pt. 2) **91**:470 (Nov.) 1933.

The classification of mental disease associated with presenility is obscure and uncertain. The cases of five women showing similar symptoms are described. Halberstadt hesitates to state that they constitute a morbid entity or a clinical variety of a larger group. All showed delirium of slight degree, which was fleeting and did not dominate the picture. The most marked characteristic was negativism and self-depreciation. The patients were puzzled rather than truly disoriented. There was marked tendency to resistance and contrary reaction. The psychosis evolved in a gradual manner toward a state of intellectual enfeeblement, and anxiety gave way to negativistic tendencies. The process often lasted for years, with short remissions. Antitonic dysphrenia is included among the demential forms of involutional melancholia but differs in some respects from the other types, because of the delusional element.

MOORE, Boston.

FALLACIES OF THE SENSES. T. BURROW, Scientia **38**:354 and 432 (May-June) 1935.

Disorders of adaptation affecting the relation of man to his social environment are due to widespread discrepancies in physiologic function. Man's internal reactions to stimuli are not only primary responses of the total organism but secondary, or restricted, patterns of reaction "which interfere with the organism's balanced reaction as a total behavior-process." Man is related to his environment not only through the function of the peripheral senses but by a symbol-forming function, which is an outgrowth of the total organism. This symbolic, or cerebral, system places man in relation to "signs, images or symbols of persons or things, not

directly in relation to actual persons or things themselves." Through overemphasis, this secondary system has come to assume dominance over the primary system, so that feeling and thinking are attached to signs and symbols of persons and objects in the external world rather than to actual persons and objects. Thus, there results an error of perception, since in states of emotional excitement a person is not seen, but merely "the image or connotation by which the individual is arbitrarily symbolized." Man sees whom he wants to see and fails to see what he looks at, what is before him. He becomes prey to definite fallacies of the senses," which express themselves in distorted behavioral patterns leading to serious disorder socially and individually."

In his social relationships man is completely habituated to a prevailing mode of behavior, which is not total but partitive. Physiologically, this is explained as a reflex which results in partitive responses, and this reflex system of image reactions tends to operate socially along with the reactions which affect man as a total organism. As long as the partitive responses which constitute a separate personality within the organism do not dominate or become confused with responses of the total organism man is well adapted, but when the two responses become confused "there occur those inroads upon the organism's total equilibrium which in their extreme form lead to neurosis and disorganisation.'

KAHN, Philadelphia.

INDIVIDUAL PSYCHOTHERAPY. M. MÜLLER, Fortschr. d. Neurol., Psychiat. **7**:282 (July) 1935.

In his introduction, Müller admits the impossibility of including in a single manual a discussion of the rationale and methods of all the various schools of psychotherapy and as a corollary states his intention of selecting for presentation only those methods which experience has taught him are most valuable and in which he therefore believes.

Into every form of psychotherapy the intuition, the personality and that intangible quality which may be termed the "art" of the physician enter as inevitably as does his more formal skill or knowledge. Moreover, only he who has experienced, fathomed and solved his own conflicts and has thereby acquired tolerance and breadth of vision is equipped to deal with the troubled minds of his fellowmen. Further, the true psychotherapeutist must possess a certain sympathetic, humane eagerness to understand his patient and must not ever consider the latter simply another "case" to be diagnosed and "treated." The bond of sympathy between the patient and the physician, however, must never be permitted to ripen into actual friendship for this reason: Every form of psychotherapy partakes partly of the nature of a contest, and in this contest the physician must ever be free to assert his dominance. The successful therapeutist must therefore keep a certain distance and not permit his own attachments to complicate the problem of therapy.

Müller divides psychotherapy into two main types: individual and collective. The latter includes all forms of institutional or social therapy the objective of which is to change the patient's milieu. By individual psychotherapy, on the other hand, is meant the direct personal influence of the physician on the patient. In many cases the two types of therapy are inextricably intermingled, but the distinction between the two is of some pragmatic and pedagogic value.

Individual psychotherapy is most useful in the treatment of the various neuroses, but in certain modified forms it also has its applications for the psychoses. Individual psychotherapy employs in purest form the "transference"—a phenomenon the importance of which was first elucidated in psychoanalytic theory. By "transference" is meant that emotional relationship between the patient and the physician which develops during the course of every extensive individual psychotherapeutic procedure. The "transference" itself as a rule springs from certain unconscious erotic strivings of the patient and can, according to Freud, be traced in every case to the patient's infantile fixations and love objects. The latter, being reactivated in the course of the therapy, are then identified not with the physician's person but with the patient's fantom-like idealization of his therapeutist. The transference

may become a powerful tool in the hands of the physician, but he must be careful to use it properly and resolve it at the end of the therapy or else run the risk of a permanent personal fixation.

Individual psychotherapy may be subdivided as follows: (1) revealing (*aufdeckende*) psychotherapy, represented solely by psychoanalysis, and (2) concealing (*zudeckende*) psychotherapy, i. e., hypnosis, suggestion and persuasion.

Müller contrasts the possible application of these forms of therapy in the case of a girl aged 17 whose chief complaint was that of bed-wetting since the age of 7. Somatic factors were excluded, and the history, as given by the patient and her relatives, furnished no clue as to a possible neurotic cause for the symptom. It was obvious, then, that the patient's motivations and conflicts would have to be sought not in her superficial, conscious thinking and willing but in her unconscious. It is the prime assumption of psychoanalytic theory that neurotic symptoms are not the result of conscious conflict but have their roots in unconscious motivations which, because of their painful nature, are "repressed" from consciousness by the "censor." These processes may be uncovered only by the method of Freud, but the technic of this method requires years of study and special application in addition to a personal analysis. Briefly, the method employs both so-called "free association" and dream analysis, the latter being particularly significant because of the comparative weakness of the censor during sleep. Always, however, the accuracy of interpretation of the material lies not in the theoretical formulations of the practitioner but in the subjective reactions and feelings of the patient. Also, one does not begin in a particular case by attempting a direct analysis of the presenting symptom, else the censor would immediately oppose insuperable resistance. One must, instead, approach the underlying mechanism in a much more indirect and laborious fashion.

In the case of the patient mentioned it finally appeared from an analysis of free associations and dream data that since early childhood she had continually wished to have masculine instead of feminine attributes and had, in fancy, conceived herself to have been castrated. Despite this explanation the patient nevertheless continued to hope that she might yet acquire the male organ. When, however, in later life she was faced with the undeniable evidence of continued femininity, she was forced to repress her wish for sex metamorphosis. This wish, however, persisted in her unconscious and sought expression in a number of indirect ways. For one example, she disliked handiwork and other feminine pursuits; for another, she was constantly in conflict with men in her environment. Ultimately, the connection between her persisting enuresis and her "penis-wish" was finally discovered in a series of childhood incidents: She had repeatedly witnessed a male playmate in the act of urination and had under those circumstances felt most keenly her own lack of the male organ. She had, moreover, in ignorance of the real sexual meaning of the penis, attributed to it the primary function of urination. In later life, therefore, she expressed her repressed wish for the possession of a penis by fulfilling her childish fantasies of its function.

This case, then, illustrates a fundamental principle: The neurotic symptom is a compromise between a libidinous drive on the one hand and the censoring and guarding faculties of the personality on the other. The symptom consummates in masked and altered form the repressed drive and at the same time, through its painful character, fulfils the demands of the patient for self-punishment. As to the therapeutic value of psychoanalysis, the very process of bringing these hidden conflicts to consciousness during the course of the analysis itself releases some of the pathogenic tension and resolves some of the symptoms. Further therapy, however, is obviously necessary: The force of the wishdrive (*triebwunsch*) must be shunted to more favorable compromises, and in this process the transference plays its most useful rôle. Thus, in the case cited the presenting symptom, the enuresis, must be controlled and the patient must be reconciled whole-heartedly to her fated femininity.

In contrast to this technic are the methods of the "concealing" psychotherapy, which aim primarily for a direct investigation and control of the presenting

symptoms as such. Thus, the psychotherapeutist, in treating the patient whose case is cited, would in an authoritative manner assure the patient that her symptoms had no basis in any somatic illness and would perhaps reenforce this suggestion by the prescription of special diets, medicaments or the employment of faradization. By these means the leading symptom might be controlled, although the patient's underlying conflicts would in no way be resolved. Again, if the patient's suggestibility indicates, the physician might employ hypnosis—a state in which the patient's attention is most firmly fixed and her psychic processes brought most easily to the will of the hypnotist. But it must be realized that hypnosis also has its limitations; no suggestions contrary to the personality of the patient will take hold, or, in the words of Kronfeld, no imbecile will be educated or paranoiac cured.

Other methods of concealing therapy are the "logical discussions" of Stransky and the "persuasion" of Dubois. In the latter an attempt is made to divorce the patient from his symptoms by explaining to him the unseemliness, injuriousness and adverse social consequences of his behavior. However, it is probable that whatever favorable results are obtained by this method may be attributed to the effects of transference and suggestions, since in the majority of cases the patient has long been aware of the information imparted and has despite this demonstrated his lack of power to change his behavior. Nevertheless, persuasion is undoubtedly of value for the more intellectual and cultivated patients, in whom primitive drives are less potent.

Since in final analysis all forms of concealing psychotherapy seem based on suggestion, it is of interest to investigate the dynamics of this process. It is probable that suggestion reenforces certain reactive tendencies already present as a result of unconscious wishes and at the same time renders deeper repression of these wishes possible. Thus, in hypnosis, the ego of the patient becomes identified with the personality of the hypnotist and partakes of the latter's processes of will, which may then be used to reenforce the needed repressions in the patient. Here, however, is also revealed the weakness of all concealing psychotherapeutic methods: The conflict is not resolved and therefore retains its pathogenic power, which if the repression is ever again relaxed may express itself in the recurrence of the old symptoms or in the formation of new symptoms. The concealing psychotherapy, then, in contrast to psychoanalysis, may produce quick and spectacular, but not always permanent, results, although the various forms of the former are obviously more economical and more easily applicable by the general physician for the production of immediate therapeutic effects.

Finally, a combination of the two types of therapy may be employed: A preliminary understanding of the illness obtained through a partial analysis is used as a basis for more immediate suggestive therapy. It may be stressed in conclusion, however, that an orthodox psychoanalytic technic is essential for a complete understanding of the nature of the neurotic conflicts in any particular case.

MASSERMAN, Chicago.

TYPES OF ENDOGENOUS PSYCHOSIS IN PERSONS OF THE NORDIC RACE. H. BURKHARDT, Ztschr. f. d. ges. Neurol. u. Psychiat. **153**:165 (July) 1935.

The types of psychosis in fifty-nine persons of the Nordic race were studied. Burkhardt used strict somatic criteria in choosing his patients (color of hair, eyes, height and cephalic index). The families of the patients had lived in Schleswig-Holstein for a few generations. In fifty cases the diagnosis was unquestionably that of schizophrenia. In nine cases there were unimportant atypical features in the schizophrenic syndrome. Autism was a marked feature in most (forty-eight) of the cases. Catatonic and paranoid tendencies were absent. Extroversion was not present in the make-up of these patients prior to the onset of psychosis. Periodic or cyclic schizophrenia was not found. Burkhardt calls attention to the complete absence of cyclothymic reactions. He notes the relative freedom in the cases in this series from markedly atypical reaction patterns and, especially, the

absence of affective liability. Endocrine disorders were not present. He points out that the predominance of autism confirms the opinion that the Nordic mind is more or less self-sufficient and does not permit undue modification and influence by external factors.

SAVITSKY, New York.

PROGNOSIS IN THE SCHIZOPHRENIC FORM OF DEMENTIA PARALYTICA. L. von ANGYAL and K. GYÁRFAS, Ztschr. f. d. ges. Neurol. u Psychiat. **153**:753 (Sept.) 1935.

Angyal and Gyárfas found a clinical picture characteristic of schizophrenia in twenty-five of seven hundred and ten cases (3.52 per cent) of dementia paralytica in a Budapest hospital after 1926. They followed the further course of the illness in twenty of these cases and in three others from another hospital. They divide the schizophrenic form of dementia paralytica into three subgroups: 1. The process of dementia paralytica precipitated true schizophrenia in fifteen cases. The two disease processes coexisted, though schizophrenia in some way became manifest as a result of dementia paralytica. In five cases there were definite premorbid schizoid tendencies, and in seven there was a familial incidence of schizophrenia. In ten instances features characteristic of schizophrenia were evident before the fever therapy, and in five they became manifest during the hyperpyrexia. In most of the cases the clinical picture was that of a paranoid hallucinatory syndrome. Catatonic features were present in only one case. In most instances, when the symptoms of dementia paralytica disappeared the schizophrenia continued to progress. In seven patients no organic reaction pattern was observed. The schizophrenic symptoms disappeared in three cases as intellectual enfeeblement progressed.

2. Reactions characteristic of schizophrenia were noted in persons who apparently had recovered from a previous attack of a condition suggesting dementia praecox. The process of dementia paralytica in these cases precipitated an exacerbation of the schizophrenic process with, however, none of its malignant features. The authors had only two cases of this type. Their conclusions regarding the prognosis for this type were tentative. The outlook in cases of this type depends on the severity of the dementia paralytica. If this improves the schizophrenic syndrome also disappears.

3. In six cases there were transitory paranoid hallucinatory states resembling schizophrenia, which belonged, however, to the group of symptomatic schizophrenic reactions. The mental changes usually disappeared with the onset of remission of the dementia paralytica. In one case this episode appeared before fever therapy, and in five, during or after this treatment. The delusional experiences were evidently projections of awareness of intellectual and somatic deterioration. Occasionally expansive tendencies were present. Four of these six patients had complete remissions, with no recurrence after from two to nine years. One patient died of a somatic infection six months after treatment, and one became worse. A premorbid schizoid make-up was present in two instances.

Differences of opinion in the past regarding prognosis in cases of this type were due to failure to distinguish between the different forms of schizophrenic reaction patterns. The general impression is that the process of dementia paralytica in cases in which there is a clinical picture of schizophrenia is mild and more benign.

SAVITSKY, New York.

Diseases of the Brain

SYPHILITIC PSEUDO-BULBAR PALSY WITH CONVULSIVE WEEPING. L. J. KARNOSH and WILLIAM H. CONNOR, Am. J. Syph., Gonor. & Ven. Dis. **20**:115 (March) 1936.

Syphilitic pseudobulbar palsy is rare and when present is often considered to be a manifestation of dementia paralytica. The lesion appears to be a bilateral implication of the internal capsule; when the geniculate portion is involved

grimacing is likely to occur. The control of the facial muscles seems to spring from two sources or to travel by two routes, since in cases of this disease voluntary facial control is often dissociated from emotional facial response. These emotional responses, whether of joy or sorrow, often fail to reflect the actual emotion of the patient. Karnosh and Connor describe two cases, both in men aged 40, with meningovascular syphilis of the central nervous system. Each patient had right hemiplegia, with aphasia and facial grimacing. One patient had bilateral facial paralysis for voluntary movements, the other weakness of the right side of the face for voluntary movements. In each case, however, there was extensive facial movement during the emotional paroxysms. One patient had uncontrollable spells of weeping, with every facial appearance of grief; the other had bouts of unprovoked laughter or crying. Therapy with a combination of arsenic and bismuth produced improvement in the pseudobulbar and emotional symptoms in both cases.

DAVIDSON, Newark, N. J.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSTIC DATA ON SPECIFIC TYPES OF SUPPURATION IN THE PETROSAL PYRAMID. SAMUEL J. KOPETZKY, Arch. Otolaryng. **22**:403 (Oct.) 1935.

Osteitis and osteomyelitis must be differentiated clinically. Osteomyelitis may be hematogenic or otogenic. The former, most frequent in the very young patient, has a clinical picture of general infection. Otitic phenomena are present but do not dominate the picture. The lesions are usually bilateral, with meningitis as the end-result. Otogenic osteomyelitis, on the other hand, more clearly takes the course which shows it to be the sequela of otitic infection. It occurs at any age, usually during the course of purulent otitis media, after the acute phase has passed. There are signs of renewed acute infection, local edema and pain in the distribution of adjacent nerves. If the disease is allowed to progress, death ensues from sepsis, pulmonary complications or meningitis. Roentgenography is an aid in establishing the diagnosis. The lesions are most evident in the occipital or the parietal bone. Osteomyelitis occurs only in pneumatized petrous tips. Coalescent osteitis of the temporal bone is a complication of infection of the middle ear, just as is coalescent mastoiditis. Frequently the disease extends outward to the tympanum, epitympanum and mastoid process, resulting in simple mastoidectomy before the characteristic signs and symptoms of petrositis appear.

Diagnosis of the coalescent type of petrositis resolves itself into: (1) the determination of its presence, (2) the determination of its location within the petrous perilabyrinth, (3) evaluation of the clinical picture and (4) differential diagnosis from other conditions. The most constant sign is intra-orbital and supra-orbital pain, due to involvement of the first branch of the fifth nerve. The next constant sign is continuation or recurrence of the purulent process from the tympano-mastoid region, and finally, there is always fever, which takes a moderately septic course.

Almour has suggested a division of the types of infection of the petrous bone into: (1) posterior petrositis, subdivided into posterosuperior, postero-inferior and postero-internal petrositis, and (2) anterior petrositis, subdivided into supracochlear, infracochlear, pericarotid and peritubal lesions and apicitis. In the first group transient vertigo, nystagmus and nausea are noted. In the second group facial palsy suggests a supracochlear lesion. Involvement of the vagus nerve suggests an infracochlear lesion. In all cases of anterior petrositis profuse purulent otorrhea is present and continues to progress while the mastoid disease rapidly heals. In the posterior type there is no evidence of healing of the mastoidectomy wound, but the drum and tympanic cavity may heal completely, especially in postero-internal and postero-inferior petrositis. In inspecting the mastoidectomy wound in a case of suspected petrositis, one should first look for the presence of a fistula and, if necessary, should improve drainage. In the posterior type this may be done through a simple mastoidectomy wound. In the anterior type radical exposure of the tympanic cavity must be made. When a fistulous tract is not demonstrable the encapsulated pus must be located.

HUNTER, Philadelphia.

INVOLVEMENT OF NERVOUS SYSTEM IN TRICHINIASIS. H. HOUSTON MERRITT and MILTON ROSENBAUM, J. A. M. A. **106**:1646 (May 9) 1936.

Merritt and Rosenbaum encountered two patients with neurologic complications of trichiniasis in the neurologic unit of the Boston City Hospital. The diagnosis in these cases was made with great difficulty. The involvement of the nervous system in trichiniasis may simulate polyneuritis, acute anterior poliomyelitis, encephalomyelitis and, rarely, meningitis. Cases in which there is presented weakness of the muscles of the trunk and extremities with absence of reflexes are the most common. The evidences in such cases vary from complete paralysis with absence of reflexes to absence of reflexes without muscular weakness. Nine cases in which the nervous system was studied at necropsy are recorded in the literature. The pathologic mechanism of the production of neurologic symptoms in cases of trichiniasis is not entirely clear. It can be readily understood how the inflammatory nodules in the brain and cord can produce symptoms, and it is also possible that small cerebral or meningeal vessels may be occluded by the organisms or by emboli from cardiac involvement and produce cranial nerve palsies and other focal signs. But the mechanism of the production of symptoms of generalized weakness and absence of reflexes is not understood. It has been thought that these symptoms may be due to involvement of the nerves by the trichinae or a toxin produced by them. This is supported by the finding of altered electrical reactions. It has been suggested that these symptoms may be due to the trichinous myositis. This is not a satisfactory explanation, however, since the reflexes are not lost so early in other forms of myositis. Trichinae have been observed occasionally in the spinal fluid of patients with trichiniasis, with or without nervous symptoms. In addition, lymphocytes have been noted in the fluid in several cases. Merritt and Rosenbaum examined the fluids from eleven patients with trichiniasis, and the results were entirely within normal limits with regard to the pressure, cell counts, protein content and colloidal gold and Wassermann reactions. No embryos were observed. Normal results were also reported by others. The reports of the finding of trichinae in the fluids are chiefly in the older literature. In recent years more reliance has been placed on the cutaneous test and the biopsy of the muscles, and the fluids are therefore probably not searched as carefully for these organisms. It is necessary to differentiate trichiniasis complicated with neurologic disturbances from (1) polyneuritis, (2) poliomyelitis, (3) encephalitis or encephalomyelitis, (4) meningitis, (5) dermatomyositis and (6) periarteritis nodosa. The diagnosis of trichiniasis can usually be established by the history of ingestion of pork, eosinophilia in the blood (which may not develop until late, however), the cutaneous test and biopsy of muscles. The cerebrospinal fluid is usually normal and helps to exclude poliomyelitis, encephalitis and meningitis. Since cutaneous lesions may be present in trichiniasis, the condition in which muscular weakness is presented may be confused with dermatomyositis. It is differentiated, however, by the absence of widespread subcutaneous edema, the history of ingestion of pork, cutaneous tests and biopsy. Patients with periarteritis nodosa may have polyneuritis with muscular weakness, absence of reflexes and eosinophilia in the blood. The differential diagnosis in these cases depends on palpation of the arterial nodules or biopsy of them. The prognosis in the cases in which only muscular weakness or absence of reflexes is presented is good. The patients practically always recover, with slight or no residual manifestations. The outlook is much more serious in the cases in which mental symptoms or signs of focal lesions in the central nervous system are presented. EDITOR'S ABSTRACT.

DISTURBANCE OF CEREBRAL FUNCTION IN CONCUSSION. C. P. SYMONDS, Lancet **1**:486 (March 2) 1935.

Symonds believes that the term concussion may usefully be retained for all the degrees and phases of traumatic unconsciousness due to disturbance of cerebral function of uniform character but varied depth. As an example of a minor con-

cussion he mentions a man who suffers a blow on the head and yet continues to play football, though with no memory of what he has been doing. In jacksonian phraseology, the highest level of cerebral function has alone been affected. At the other end of the scale there is the patient who lies in a state of vegetable inactivity, perhaps for several days, unresponsive except to painful stimuli, taking food from a spoon automatically and passing urine and feces into the bed. All levels above that of the vegetative and nocireactive functions are out of action. Symonds compares the phenomenon of concussion with that of an epileptic explosion. He believes that the disturbance of function underlying traumatic unconsciousness is probably of the same general nature as that which results from the epileptic explosion.

Symonds cites Russell, who attempted to correlate the duration of unconsciousness after an injury with the resulting disability. Russell found that of patients who were unconscious less than an hour 90 per cent returned to work in less than six months, of patients unconscious more than an hour but less than twenty-four hours 84 per cent returned to work in less than six months and of patients unconscious more than seventy-two hours 66 per cent returned to work in less than six months. From these figures Symonds deduces that a long duration of unconsciousness does not necessarily imply a long duration of disability. He objects to the time-honored tradition which inculcates the need of three weeks in bed for any patient who has suffered concussion. This takes no account of the patient who has suffered injury to the head without concussion and is liable to sequelae which may demand prolonged rest. Another objection is that a patient who has had concussion may have suffered no lasting damage to the brain and may recover fully within a few days after regaining consciousness. It seems more reasonable to Symonds to proceed on the plan of dealing with each condition on its merits. In the case of mild concussion the patient should be kept in bed for twenty-four or forty-eight hours, and then, if free from symptoms, he should be allowed gradually to submit himself to more physical effort and mental stress. In cases of more severe concussion the duration of rest should be longer. If the patient from the first or at any time later exhibits symptoms such as headache, dizziness or mental debility, rest should be increased and prolonged and convalescence retarded until the symptoms have disappeared. This rule should apply whether concussion has occurred or not.

WATTS, Washington, D. C.

PARINAUD'S SYNDROME FROM HYPERTONIA OF THE INFERIOR OBLIQUE MUSCLE AND SPASM OF THE LEVATOR MUSCLE, IN A PATIENT WITH HEMIPLEGIA OF THE LEFT SIDE. H. ROGER, G. E. JAYLE and J. PAILLAS, Rev. d'oto-neuro-opht. **14**:190 (March) 1936.

In the case reported in this paper there was isolated automaticoreflex paralysis of vestibular function of the clockwise and downward movements of the eyeballs. The patient, a man aged 57, was addicted to the use of alcohol and had a chancre in 1900, which was inadequately treated. The illness began with vertiginous disturbances, which culminated in a severe attack of vertigo, followed by unconsciousness, inability to speak, paralysis of the left side of the face and left hemiplegia. Thorough examination eight months later resulted in the diagnosis of Parinaud's syndrome, with spasmodic retraction of the elevators of the lids, predominating on the left side, hypertonia of the inferior oblique muscle and hemiplegia. The authors believe that complete vestibular examination, including galvanic, rotatory and caloric tests, should be made in every patient with ocular disturbances. The function of both the horizontal and the vertical canals must be investigated. In the patient under discussion it was impossible to obtain rotatory nystagmus except in the left eye, although these movements appeared spontaneously on looking laterally. Provoked vertical nystagmus could not be elicited, being replaced by horizontal nystagmus. In the light of the past history of the patient, the clinical phenomena and the vestibular anomalies, the conclusion was reached that the lesion was located in the upper part of the cerebral peduncle, bordering on the subthalamic region.

DENNIS, San Diego, Calif.

A New Parieto-Occipital Syndrome (Psychic Blindness: Disturbance of the Body Image; Loss of Central Vision). H. Hoff and O. Pötzl, Jahrb. f. Psychiat. u. Neurol. **52**:173, 1935.

Hoff and Pötzl describe in detail the case of a patient with disturbance of optic attention to the left, change in the body image and absence of central vision. These manifestations were associated with hemianopia, hemianesthesia and hemiparesis on the left side. Necropsy disclosed extensive softening involving almost the entire parieto-occipital convexity. The area of softening was wedge-shaped and destroyed all the white matter in that region, interrupting thereby the fibers of the right side of the corpus callosum for a considerable distance. The lesion extended to the occipital pole and undermined the polar portion of the right calcarine area, destroying especially the macular portion of the optic radiation on that side. The loss of central vision is attributed to the fact that in addition to the recent lesion on the right side of the brain there was also a smaller and older lesion in the forceps major of the corpus callosum, which interrupted the macular fibers of the optic radiation as they decussate from the left hemisphere by way of the splenium to the right side. The patient showed no evidence of true optic agnosia. During reading there occurred occasionally displacement of letters and words, but there were no mirror errors. Writing and drawing of geometric figures, however, was constantly interfered with by mirror tendencies. The mirror tendencies during writing with the right hand were explained by peculiarities of gesture and by a tendency to symmetrical associated movements with the left hand. The latter occurred only when the right arm was held down. At such times speech by gesture was immediately transferred to the left hand without the patient's noticing the difference. This shunting process is attributed to the almost complete intactness of the thalamic region and of the basal ganglia. A greater concentration of activity of the left side of the brain for the right hand "chokes up" the pathways conveying impulses for symmetrical associated movements which, under these circumstances, can reach the left hand, thus releasing the impulses and directing them to the right hand. It is also conceivable that the source of impulses for the symmetrical associated movements is the simultaneous stimulation of identical points in the right cerebral hemisphere during writing and drawing. Since the motor area of the right side was destroyed and the cephalic portion of the corpus callosum damaged by the older lesion, this theory of the source of impulses for symmetrical associated movements is not tenable. It is more likely that there occurred a dissociation of the proprioceptive system in the sensory sphere, the principal part of which is contralateral, whereas the remaining part destined to supply sensation to the homolateral side of the body remains, under ordinary conditions, in the background (overlapping of the sensory sphere in the sense of Dusser de Barenne).

On the basis of proprioceptive optical images the patient was fully capable of spatial orientation of past situations. As far as the external world was concerned, however, she could orient herself only upward, downward and to the right, but not to the left. When she was asked to point to the left she made only circular movements which corresponded fully to the mirror tendencies which she displayed during writing and drawing. The body image was similarly limited on the left side. The patient was unaware of the existence of her left hand or of her left eye and was uncertain of the position of the tongue in the left side of her mouth. Most frequently she experienced the sensation of having only the right hand, although occasionally she stated that she knew that she had two hands; she constantly confused left and right, and on being shown her left hand she never identified it as her own. Frequently she showed a tendency to look away from her left hand when it was shown to her, and when the examiner insisted that she look at it she became disgusted and explained: "Away with the hand!" —"Why have I three hands? I do not feel the hand."—"I am not the mistress of my own hand." On direct questioning, she denied the sensation of feeling as though the left hand had been amputated; only on one occasion did she admit a "strange feeling" on one side of the body.

The limitation of the body image to the left, without fantom formation and without hallucinations of movement, is attributed by Hoff and Pötzl to total destruction of the entire sensory area on the right side of the brain, with destruction of the callosal fibers on the right side and intactness of the thalamus and basal ganglia.

KESCHNER, New York.

THE TOPICAL DIAGNOSIS OF TUMORS OF THE BRAIN. E. C. BENDA, Monatschr. f. Psychiat. u. Neurol. **89**:53 (June); 105 (July) 1934.

The clinical pictures associated with tumors of the brain in certain locations were studied in one hundred cases in which the diagnosis was verified by operation or by postmortem examination. Particular attention was devoted to the clinical course and to the symptoms regarded as of special diagnostic importance.

In a group of ten patients with neurinoma of the auditory nerve the illness developed slowly, medical aid being sought on an average of from three to six years after the first symptoms had been noted. There was gradually increasing dizziness or impairment of hearing and uncertainty of gait. Examination disclosed partial or complete deafness, diminution or abolition of the response to vestibular stimulation, spontaneous nystagmus toward the affected side and involvement of the trigeminal nerve, which was sometimes manifested solely by a diminished corneal reflex. Papilledema was observed in nine patients and paresis of the facial nerve in six. Headache and vomiting occurred only in the later stages of the illness. In patients with other types of tumor located in the cerebellopontile angle, the course was frequently more rapid than that noted in patients with neurinoma of the auditory nerve, and headache and visual disturbances were earlier symptoms. Later the two groups presented similar clinical pictures, though general disturbances, such as drowsiness or apathy, were more prominent in the former than in the latter. In both groups the head tended to assume a fixed posture. Since syphilis must be excluded, it was usually necessary to examine the cerebrospinal fluid. For this purpose cisternal puncture was recommended. Encephalography is dangerous in such patients and should be avoided.

There were two patients with tumor of the fourth ventricle. As a rule, it is difficult to diagnose this condition, but an acute exacerbation of the symptoms, a state of collapse, tonic convulsive attacks or attacks resembling petit mal may help to differentiate it from cerebellar tumor.

Tumor of the vermis of the cerebellum tended to occur in youthful persons and to develop rapidly. In some cases there were marked symptoms a few weeks after the onset of the illness. Headache, vomiting and ataxia were early features. The posterior part of the skull was sensitive to pressure, and there was fixation of the head, which was inclined to one side or retracted. Some patients showed hypotonia of the extremities with increased reflexes. Papilledema was regularly observed. Spontaneous nystagmus did not occur as a rule till late in the illness. Hearing was not impaired. The response to vestibular stimulation was usually increased on both sides. In cases of tumor of the cerebellar hemisphere there was often unilateral involvement of certain cranial nerves, particularly the facial or the trigeminal nerve, but apart from this the clinical pictures were similar to those associated with tumors of the vermis.

In the study of patients with tumor of the frontal lobe, those in whom the growth involved the central convolutions were excluded. Mental changes were prominent in this group. There were impairment of memory and comprehension, diminished activity and slowness of thought and speech. Two members of the group, which included twenty-three patients, presented clinical pictures suggestive of dementia paralytica, and only one showed typical facetiousness. Manic-like states tended to occur in patients in whom the tumor was located posteriorly and involved the floor of the third ventricle. Almost all the patients displayed incoordination, which was difficult to differentiate from the ataxia caused by a cerebellar tumor. Dizziness, fixation of the head and slight ptosis or protrusion of the

eyeballs were common. While headache was of frequent occurrence, it was entirely absent in certain cases. It was likely to come on suddenly in migraine-like attacks. Only one patient showed nystagmus. Papilledema was often observed, but it was usually unilateral or more pronounced on one side than on the other. Atrophy of the optic nerve with disturbances of the visual field was an early and frequent feature. The results obtained on testing the sense of smell were too unreliable to be of definite value. The frontalis reflex, which is elicited by striking the supra-orbital ridge near the point of exit of the supra-orbital nerve, was often increased. A grasping reflex was occasionally noted in a torpid patient. Reflex anomalies in the extremities were common and were the more prominent the nearer the tumor was to the precentral convolution. Benda does not believe that the type of frontal tumor can be determined from the clinical picture or course of the illness. However, a dural endothelioma tends to cause more marked general symptoms than a glioma of the white matter, and the latter is likely to lead to more pronounced weakness, exhaustion and impairment of memory. Atrophy or neuritis of the optic nerve points to a tumor at the base of the frontal lobe. Clinically, it was frequently impossible to differentiate such a tumor from a suprasellar tumor that had extended anteriorly.

ROTHSCHILD, Foxborough, Mass.

CHOREIFORM SYNDROME OF THE RIGHT UPPER EXTREMITY AS A MANIFESTATION OF MONOSYMPTOMATIC CEREBRAL SYPHILIS. FRANZ T. MÜNZER, Ztschr. f. d. ges. Neurol. u. Psychiat. **152**:12, 1935.

Reports of only six cases of chorea as a symptom of syphilitic involvement of the striopallidum were found in the literature. The case of a man aged 45 who acquired syphilis thirteen years before is described. Characteristic movements of a choreiform nature developed, which remained localized to the right upper extremity. In addition, there were hypotonia of this extremity, mimetic paresis of the right facial nerve, paresthesia of the lateral aspect of the thumb and a slight increase in the right achilles tendon reflex. The spinal fluid presented findings typical of cerebral syphilis. The localization is postulated as being in or near the left optic thalamus. The quick response of the condition to antisyphilitic treatment and the absence of hereditary predisposition to chorea speak for a syphilitic etiology.

MICHAELS, Boston.

GENETIC AND CLINICAL ANALYSIS OF THE TORSION SYNDROMES. J. A. BEILIN, Ztschr. f. d. ges. Neurol. u. Psychiat. **152**:126, 1935.

Two Jewish boys aged 10 years presented torsion dystonic features of the left extremities, and with the discovery of their relationship, Beilin was led to examine the familial histories. Six generations consisting of 104 individual members were collected, of whom 42 were personally examined by the author. The following anomalies were found: (1) epilepsy, 1 case; (2) migraine, 1 case; (3) spasmophilic convulsive syndrome, 9 cases; (4) short fingers, 4 cases; (5) anomaly of the fifth finger, 4 cases; (6) short stature, 10 cases; (7) tremor in various parts of the body, 4 cases; (8) hypertrichosis of the back, 6 cases; (9) nocturnal incontinence, 3 cases; (10) blue sclera, 6 cases; (11) severe concavity of the foot, 5 cases; (12) flatfoot, 1 case; (13) Babinski sign (pseudo-Babinski sign), 5 cases; (14) microcephaly, 2 cases; (15) squint, 2 cases; (16) stuttering and stammering, 2 cases; (17) hypoplasia (?) of the thyroid, 6 cases, and (18) intermarriage of relatives, 1 case. The course of the torsion dystonic elements is considered as a heterozygous recessive type without any relationship to sex. Of special significance is the longevity and abundance of children, which are striking in the family. Although a clinical relationship has been postulated between athetosis and torsion dystonia, the author does not find this to be the case in heredity. Torsion dystonia must not be confused with Wilson's disease or Westphal-Strümpell's disease.

MICHAELS, Boston.

SIGNIFICANCE OF A HISTORY OF EPIDEMIC ENCEPHALITIS (ENCEPHALITIS LETHARGICA) IN THE PATHOGENESIS AND DETERMINATION OF CLINICAL VARIANTS OF OTHER CEREBRAL AFFECTIONS: CONTRIBUTION TO THE PROBLEM OF ACQUIRED LOCAL VULNERABILITY OF BRAIN TISSUE. ERWIN STENGEL, Ztschr. f. d. ges. Neurol. u. Psychiat. **153**:425 (Aug.) 1935.

Stengel reports three cases presenting puzzling problems in pathogenesis in association with encephalitis. The first case was that of a woman aged 28, who was admitted to the clinic in May 1933, with a history of epidemic encephalitis in 1924. Immediately before her admission there was a sudden onset of signs of meningeal irritation, with herpes labialis, somnolence, a few cranial nerve signs, papilledema and pleocytosis. These changes disappeared in five weeks. Stengel concludes that this was probably another virus infection in a person who had passed through an attack of epidemic encephalitis. The previous attack of encephalitis, in his opinion, was responsible for the prominence of somnolence in the particular clinical picture.

The second case was that of a woman aged 34, who had had epidemic encephalitis (encephalitis lethargica) in 1918. The only sequel to this infection was persistent insomnia. Sixteen years later there was a sudden onset of fever, diplopia and signs of parkinsonism. Study of the spinal fluid showed the presence of an inflammatory process. A few days after the onset of these changes a marked necrotizing streptococcic angina set in. When the disease of the throat cleared the parkinsonism disappeared. Stengel believes that the transitory parkinsonism was caused by toxins from the infected throat acting on a particular part of the brain rendered vulnerable by the preexisting infection.

The third case was that of a woman aged 31, who was admitted to the clinic in January 1934. She had had an acute attack of encephalitis in 1930. Each time that she had an infectious disease the clinical changes characteristic of the acute attack of encephalitis returned. During a staphylococcic sepsis she had disturbances of the ocular muscles, mild cerebellar speech, palilalia, attacks of tachypnea, followed by protracted apnea, and excessive yawning. All these symptoms disappeared in a few months. An unusual feature of the respiratory paroxysms was their prompt appearance on lifting the head, on vestibular stimulation and on compression of the jugular vein.

The question in all these cases is whether there was exacerbation of the preexisting encephalitis or whether the clinical changes were due to an elective involvement of a previously diseased part of the brain by another infectious disease. It is impossible to rule out the possibility that the new infection caused exacerbation of the encephalitic process. The virus of epidemic encephalitis apparently persists in the brain. The later infection provokes renewed activity of this virus. Reported instances of transitory parkinsonism in association with various infectious diseases, such as those reported by Bing, may well be cases of abortive epidemic encephalitis, without signs of acute invasion. These cases illustrate the possibility of acquired vulnerability to later toxins and infection. The possibility of an acute invasion with encephalitis without clinical signs emphasizes the great difficulty in differentiating the acquired from the congenital or hereditary predisposition to disease.

SAVITSKY, New York.

Diseases of the Spinal Cord

INJURIES TO THE VERTEBRAE AND THE INTERVERTEBRAL DISKS FOLLOWING LUMBAR PUNCTURE. CHARLES N. PEASE, Am. J. Dis. Child. **49**:849 (April) 1935.

By an anatomic presentation Pease demonstrates the possibility of puncture of the nucleus pulposus, with loss of some of the disk substance, in cases in which the lumbar puncture needle is introduced through the dural sac and into the nucleus pulposus between the vertebral bodies. In cases in which the needle is introduced through the dura he outlines three possibilities: that the needle may be pushed into the venous sinusoids of the vertebral body; that it may puncture the inter-

vertebral disk, and that it may reach the vertebral facet. To reach the vertebral facet the needle must be introduced from the side. Apparently, from his conclusions little or no harm results from the needle entering the body, other than perhaps a slight localized infectious process. However, when the needle punctures the intervertebral disk there may be a definite loss of disk substance with a narrowing of the intervertebral space. On the basis of these findings Pease explains the occurrence of severe pain in the back at the site of the puncture after lumbar puncture. He believes that the treatment should consist of absolute rest for a time, including simple rest in bed for patients with mild involvement and hyperextension on a Bradford frame for those with more severe manifestations. In one instance he thought that it was necessary to perform a fusion operation to relieve the pain. The symptoms were pain in the low part of the back, at the site of puncture, associated with limitation of motion of the lumbar portion of the spine and weakness of the muscles of the back. In some cases difficulty in walking and pain down the thighs were present.

WAGGONER, Ann Arbor, Mich.

POLIOMYELITIS: II. THE BULBAR TYPE. JOHN A. TOOMEY, Am. J. Dis. Child. **50**: 1362 (Dec.) 1935.

Toomey reviews a previous paper in which he stated that the mechanism of the spinal type of poliomyelitis is spread of the poliomyelitis virus from the gastrointestinal tract to the "thoraco-lumbar outflow of the sympathetic system" and that the virus eventually reaches the cord by spreading along the sympathetic nervous system. A series of cases is presented in which bulbar symptoms were noted. He assumes that the virus has a definite affinity for gray fibers and states that when the virus is "taken up by the gray-fibered axons [it] travels . . . in a medullated nerve only to spill over and in a bizarre fashion to involve contiguous territory of unmyelinated character when the nerve loses its myelin sheath." He has produced experimental bulbar poliomyelitis by injecting the virus into the vagus nerve and assumes that in a certain percentage of cases the virus of poliomyelitis spreads up the vagus nerve from the gastro-intestinal tract to involve the vasomotor nuclei and, by contiguous extension, other structures, which may become involved later. The cases described first showed involvement of the vagus mechanism.

WAGGONER, Ann Arbor, Mich.

THE SEVENTH NERVE AS A POSSIBLE PATHWAY FOR THE TRANSMISSION OF THE VIRUS OF POLIOMYELITIS. JOHN A. TOOMEY, Am. J. Dis. Child. **51**:58 (Jan.) 1936.

Toomey assumes that the virus of poliomyelitis enters through the gastrointestinal tract and from there spreads to the spinal cord by way of the sympathetic nervous system. He presumes that the bulbar type of the disease can be explained by spread of the virus from the gastro-intestinal tract to the medullary area by means of the vagus nerve, further involvement, of course, occurring as the result of spread of the infection. He assumes that the virus is absorbed by unmedullated fibers and states that since "each of the papillae or taste buds situated in the tongue has unmedullated fibers inside its cuplike excrescence . . . it is possible that the virus could be absorbed by the end-fibers of the chorda tympani nerve and pass by way of this nerve to the medullary area to involve the nucleus of the seventh nerve." He describes the possible routes for spread of the virus and cites illustrative cases. In the cases in group 1 he assumes that the virus was spread by way of the chorda tympani nerve to the nucleus salivatorius adjacent to the nucleus of the seventh nerve. In seven cases in his series he believes that the spread occurred in this manner. In group 2 he states that the virus spread along the axis-cylinders of the chorda tympani and the seventh nerve to the nuclei and spilled over in the medullary area, with subsequent involvement of the sixth nerve. There were two cases of this type in his series. In group 3 presumably the virus spread to the other cranial nuclei from the nucleus of the seventh nerve, the patient show-

ing more objective evidence of disease and being more severely ill. Two cases of this type were noted, in one of which the outcome was fatal. In group 4 the virus presumably spread to the nucleus of the seventh nerve, where it might spill over and irritate the pyramidal tracts. Toomey states that crossed facial palsy would result from such a lesion. There were six cases of this type in this series; one patient died a few hours after admission to the hospital. He states that in this case the condition may have been tuberculous meningitis. In group 5 he assumes that a lesion of the seventh nerve may be associated with lesions of somatic nerve fibers in the spinal cord. There were six cases of this type; all the patients survived. Toomey has done experimental work on Macacus rhesus monkeys and concludes that the experiments performed suggested that the virus may travel along the chorda tympani nerve to the superior salivary nucleus and from there to the nucleus of the seventh nerve in the medulla.

WAGGONER, Ann Arbor, Mich.

CHANGES IN THE TYPE OF LANDRY'S PARALYSIS. TOSHIWO TANAKA, Am. J. Dis. Child. **51**:239 (Feb.) 1936.

Tanaka reports fourteen cases of Landry's paralysis, four of which occurred in 1931, two in 1932, three in 1933 and five in 1934. The patients who were seen first showed evidence only of marked ascending paralysis, followed by atrophy of the muscles innervated by the spinal nerves but no symptoms of radiculitis or encephalitis. These symptoms persisted for many months. Patients seen later showed a milder degree of paralysis and atrophy of the muscles but also evidence of irritation of the nerve roots. These patients recovered in a shorter period. In the most recent cases reported there were also symptoms referable to the cranial nerves. In these later cases the involvement of the spinal nerves and nerve roots was mild and disappeared in a short time, while the involvement of the cranial nerves was most prominent and severe. Tanaka considers the possibility that in cases of Landry's paralysis occurring in Yamaguchi province the etiology may not be the same as that in cases of anterior poliomyelitis and epidemic encephalitis and that in his series of cases there may be some direct relation to influenza. Most of the cases reported occurred during the winter, in contrast to the usual history of poliomyelitis, which occurs during the warmer seasons. Tanaka concludes that the type of disorder noted during the past four years has progressed gradually from involvement of the peripheral nerves to that of involvement of the central nervous system.

WAGGONER, Ann Arbor, Mich.

DIAGNOSIS OF NEUROGENIC LESIONS OF THE URINARY BLADDER BY CYSTOMETRY. J. M. MCCAUGHAN and J. H. HERSHEY, Arch. Surg. **30**:956 (June) 1935.

Cystometric observations of the urinary bladder in dogs were made to determine disturbance of vesical physiology caused by experimental neurogenic lesions. Section of the sympathetic, parasympathetic or pudic nerve supply or of the spinal cord below the lumbar outflow did not significantly alter the character of the cystometric curves. Transverse division of the spinal cord above the lumbar outflow produced the typical picture of "cord bladder" clinically, i. e., a marked increase in vesical capacity with very low intracystic pressure. These results confirm the views of others on the value of cystometry clinically.

SPERLING, Los Angeles.

THE DEVELOPMENT OF NEUTRALIZING SUBSTANCES FOR POLIOMYELITIS VIRUS IN VACCINATED AND UNVACCINATED INDIVIDUALS. W. LLOYD AYCOCK and C. C. HUDSON, New England J. Med. **214**:715 (April 9) 1936.

During the summer of 1935, because of the unusual prevalence of poliomyelitis in North Carolina vaccination, which had been recommended as a preventive measure, was used to a varying extent in a number of localities. Tests to determine

whether a neutralizing substance was produced were made on the blood of twenty-eight persons before and after vaccination, 46.4 per cent of whom were found to be already immune. After vaccination 75 per cent neutralized the virus. Poliomyelitis neutralization tests on thirty-five persons used as controls showed that 40 per cent were immune on the first bleeding and 62.8 per cent on the second bleeding. There was an increase in immunity in both the groups under observation—19.5 per cent in the vaccinated group and 14.9 per cent in the controls. In view of the irregularities of the neutralization test and the small number of observations it is not clear that the slightly greater advantage of the vaccinated group over the control group was the result of vaccination. The increase in immunity may have been due to natural exposure, since an increase occurred in both the vaccinated and the control group. The occurrence of eight cases of poliomyelitis in the city during the period of the experiment is evidence that the virus was prevalent there at that time.

MOORE, Boston.

SYNDROME OF DISSEMINATED SCLEROSIS DETERMINED BY SPINAL SYPHILIS. C. BALLIF and E. GLINOER, Bull. Soc. roumaine de neurol. **26**:100, 1935.

A woman began to suffer with pains in both lower extremities three years before she was observed by Ballif and Glinoer. The pains gradually increased and spread to the upper extremities. At times there was numbness. One year later, difficulty in walking appeared. Examination revealed spastic flexion paraplegia, ankle clonus, hyperactive deep reflexes and an extension toe phenomenon on the right. The abdominal reflexes were present. There was intention tremor of the hands. Superficial and deep sensibility were somewhat diminished. The pupils were normal. There were nystagmus, incontinence of urine and beginning decubitus. The Wassermann, Pandy and Nonne-Apelt reactions of the spinal fluid were positive. The benzoin curve was 1222222221000000. There were 7 lymphocytes per cubic millimeter. The pressure was 12 cm. of water. The Wassermann and Meinicke reactions of the blood were negative. Antisyphilitic and roentgen therapy were not followed with improvement in the condition.

LIBER, New York.

ANATOMIC STRUCTURE AND CLINICAL IMPORTANCE OF THE GANGLIORADICULAR NERVE. P. CORDIER, P. COULOUMA and F. VAN VARSEVELD, Encéphale **31**: 139, 1936.

The ganglioradicular nerve is defined as the nerve trunk constituted by the juncture of the spinal ganglion and the distal segment of the ventral root. It lies lateral to the biradicular nerve and medial to the funiculus, or mixed, nerve. Classic descriptions have neglected this segment of the spinal nerve. Descriptions of it vary greatly in every particular. Thus, according to Chipault and others, the ganglia are all outside the dural sac; according to Schlemm, the last three sacral and the coccygeal ganglia are within the sac, and, according to Holmdahl, only the fifth sacral and the coccygeal ganglia are within the sac.

The authors studied the anatomic features of the ganglioradicular nerve in twenty-four cadavers. In addition to the usual dissections, two special methods were used. Roentgenograms of the vertebral column were taken after the ganglia were marked in situ with lead foil or white lead. In nine cadavers gelatin, plaster of paris, barium oxide, india ink or white lead mixed with gasoline was injected into the subarachnoid space. The direction of the ganglioradicular nerve was observed to be horizontal from the first to the third cervical segment and from the second to the ninth thoracic segment. Between the fourth cervical and the first thoracic segment it is oblique caudolaterally. From the tenth thoracic nerve caudally it is increasingly oblique and tends to be vertical in the fifth sacral and the coccygeal segments. In one case the fifth, sixth, seventh and eighth cervical ganglioradicular nerves were excessively oblique and formed a distinct angulation with the corresponding radicular nerves, which were directed horizontally or cephalad. In another case the ganglia from the second to the seventh

thoracic segment were directed slightly cephalad. The thickness of the ganglioradicular nerve is not great, as it is flattened dorsoventrally. The average length is greatest in the roots of the brachial, lumbar and sacral plexuses particularly at the eighth cervical, first thoracic, fifth lumbar and first sacral segments. The smallest nerve is the first cervical (5 mm.) and the largest the first sacral (16 mm.). Each element of the ganglioradicular nerve is surrounded by a separate dural sheath, but all are joined firmly by a fibrous layer between the ganglion and the ventral root. From the fourth lumbar to the second sacral segment the dural sheath is not strongly adherent to the medial pole of the ganglion, which explains the fact that in this region an injection into the subarachnoid space made in a descending course may exceptionally reach the ganglion and separate it from its envelop, without, however, penetrating the ganglion. The ganglioradicular nerve has no arachnoid sheath. From the fifth cervical to the first thoracic nerve and from the second lumbar to the second sacral nerve, the arachnoid sheath of the dorsal root reaches the medial pole of the ganglion.

The situation of the ganglioradicular nerve with respect to the intervertebral foramen varies with the location. Laterally, the first cervical ganglion rests on the sulcus of the dorsal arch of the atlas, and the second cervical ganglion lies entirely on the dorsal arch of the axis. The remaining cervical ganglia and the first thoracic ganglion are outside the foramen. From the second to the eighth thoracic segment the ganglia are partly lateral to and partly within the foramen. From the ninth to the twelfth thoracic segment they are within the foramen, and from the first to the third lumbar segment, medial to it; the fourth and fifth lumbar ganglia are usually medial to the foramen, but they may also lie within it—the fourth lumbar in 15 per cent of the instances and the fifth lumbar in 30 per cent. The first and second sacral ganglia are partly within the foramen and partly medial to it. The third, fourth and fifth sacral ganglia are observed in only one third of the instances; they are medial to the foramen.

Lesions of the ganglioradicular nerve, like those of the funiculus, are mostly of extrameningeal, that is, of vertebral, origin. In some instances, however, the subarachnoid fluid bathes the medial pole of the ganglion; so its toxic-infectious products may be deposited there and cause a lesion, the more so as the medial pole is a dissociated zone on account of the termination of the dorsal root. It appears logical to speak of ganglioradiculitis rather than of funiculitis when one is dealing with lesions of the nerve within the intervertebral foramen in the thoracic region, the last five cervical nerves, the first two sacral nerves and even the last two lumbar nerves.

Three anomalies were noted: In one instance there was a double fourth lumbar ganglion on the right side. At the medial pole of the ganglion the ventral root bifurcated. There were thus two complete ganglioradicular nerves. In another instance the medial half of the first sacral ganglioradicular nerve on the left side was adherent to the second sacral ganglioradicular nerve. In a third instance there was a dural diverticulum, which contained the fourth sacral ganglion on the right side and the roots of the fifth sacral and the coccygeal nerves on both sides.

LIBER, New York.

MALFORMATIONS OF THE CERVICAL SPINE AND OCULAR DISTURBANCES IN THE COURSE OF SYRINGOMYELIA. H. ROGER, J. ALLIEZ and A. JOUVE, Rev. d'oto-neuro-opht. **14**:91 (Feb.) 1936.

The conclusions of Rogers, Alliez and Jouve in this paper are founded on the study of thirty-three cases. Seven cases are reported in some detail; in six there were malformations of the cervical portion of the spine. In five the following ocular symptoms were presented: congenital unilateral myopia, the syndrome of Claude Bernard and Horner, heterochromia of the iris and myosis. In a large proportion of the cases (from 25 to 50 per cent) the cervicodorsal syringomyelic syndrome was accompanied by cervical osseous manifestations, which may legitimately be con-

sidered to be congenital. The lesions of syringomyelia involving the cervical portion of the spine are accompanied by equivalent congenital disturbances, particularly ocular changes. In sixteen of twenty-five observations on syringomyelia involving the cervicodorsal region, ocular manifestations were noted (the Claude Bernard-Horner syndrome in ten instances, inequality of the pupils, slight nystagmus and bilateral myosis in two, heterochromia of the iris in two and congenital myopia in one). Comparison of the frequency of the ocular lesions and that of the spinal osseous anomalies leads to the supposition that the coexisting syringomyelic process indicates an equivalent medullary malformation. Studies made by the authors point to a teratologic origin of syringomyelia. The coexistence of congenital ocular lesions emphasizes the origin, often embryonic, of the syringomyelic process. A systematic roentgenologic examination is demanded in all cases of thermo-analgesic dissociation and in the obscure syndrome of Aran and Duchenne and will often be of aid in etiologic diagnosis.

DENNIS, San Diego, Calif.

CASE OF MULTIPLE SCLEROSIS, WITH FORMATION OF A PSEUDOSPINAL CORD BY REGENERATION. FRANK BERCHENKO, Schweiz. Arch. f. Neurol. u. Psychiat. **37**:208, 1936.

Berchenko reports the results of anatomic studies in a case of multiple sclerosis in which fatal termination occurred at 35, eighteen years after acute onset with right hemiplegia and aphasia. A tendency to spontaneous remission was noted at first, but five years after the onset flaccid paraplegia, with loss of sphincter control and total anesthesia as high as the tenth dorsal segment, developed. The spinal cord had been completely destroyed below the eighth dorsal segment. Lesions characteristic of multiple sclerosis were observed in the brain and the upper part of the cord. The destroyed portion of the cord had been replaced by fibers, myelinated for the most part, which had evidently grown in from the posterior roots to form what Berchenko terms a pseudospinal cord. In cross-section, however, this mass of fibers bore much closer resemblance to a peripheral nerve; sheath of Schwann cells were seen between the individual fibers, and no ganglion or glia cells could be demonstrated, a few granule cells containing pigment being all that remained of the cord substance. Regeneration of the posterior roots to fill the space left by removal of part of the cord has been demonstrated in the experimental animal, but, so far as the author knows, this has not previously been observed in man. The possibility that a congenital inferiority of the cord might account for the markedly destructive tendency of multiple sclerosis in this case was suggested by the observation of an area of intense gliosis similar in structure and location to that seen in syringomyelia.

DANIELS, Denver.

FRIEDREICH'S ATAXIA AND STATUS DYSRAPHICUS (WITH A NOTE ON THE RELATION OF FRIEDREICH'S ATAXIA AND DIABETES MELLITUS). F. CURTIUS, F. K. STÖRRING and K. SCHÖNBERG, Ztschr. f. d. ges. Neurol. u. Psychiat. **153**:719 (Sept.) 1935.

The authors studied the family of two sisters who had diabetes mellitus and Friedreich's ataxia. Signs of status dysraphicus were sought. This syndrome, originally described by Bremer, consists of any one or a combination of the following conditions: accessory mammary glands, pigeon breast, Horner's syndrome, differences in the breasts, kyphoscoliosis, incurvation of the small fingers, pes cavus, enuresis, spina bifida, abnormal length of the upper limbs and acrocyanosis. Signs of this constitutional disturbance were found in eighteen of the forty-one members of the family. These defects, which behaved as mendelian dominant traits, appeared often in parent and child. There was no sex linkage. The finding of similar dysraphic phenomena in association with Marie's cerebellar ataxia suggests a possible genetic relation to Friedreich's ataxia. The authors deny that status dysraphicus is an abortive form of Friedreich's ataxia. It can be considered to be a favorable genotypic milieu, or the proper soil in which Friedreich's ataxia readily develops.

Diabetes mellitus was not found in any other member of the family. The authors mention other cases in which the combination of these two diseases was present. Mere fortuitous concomitance of the two diseases is denied. A hitherto unexplained genetic relation between them probably exists. Diabetes mellitus in these cases is not of central origin, as has been shown in the case of Meltzer, who observed at necropsy definite changes in the islets of Langerhans.

SAVITSKY, New York.

Peripheral and Cranial Nerves

CAUDA EQUINA SYNDROME FOLLOWING SUBARACHNOID ALCOHOL INJECTION. LOUIS L. TUREEN and JOSEPH J. GITT, J. A. M. A. **106**:1535 (May 2) 1936.

Tureen and Gitt point out that, in describing his technic of the subarachnoid injection of alcohol for the relief of intractable pain, Dogliotti warns against possible sequels, particularly that of injury to the cauda equina. In the two cases that they describe transient relief was afforded from the pain for which Dogliotti's treatment was used. On the other hand, the bladder disturbances have persisted for more than a year in one case and for the entire period of observation (eight months) in the second case. Although the lesion produced by the alcohol was unilateral, there resulted profound incontinence of urine. In both cases 1 cc. of alcohol was injected. However, Tureen and Gitt do not find it difficult to understand how involvement of the lower sacral nerve roots occurred in their cases, especially in case 1, in which the site of injection was rather low. In both cases there was a persistent unilateral disturbance of both pain and touch sensation in the lower three or four sacral segments, although the zones of analgesia were wider than the zones of hypesthesia or anesthesia. Although this does not contradict absolutely the contention of the greater susceptibility of the pain fibers to alcohol fixation, it is a warning that the myelinated fibers are not invulnerable to this technic. The use of the larger dose of alcohol may be responsible for these results. The sciatic pain syndrome in case 1 was relieved for five weeks, but its recurrence left the patient as disabled as ever. As the injections were made relatively low, the upper lumbar nerve roots must have hardly been involved, while the lower lumbar roots were temporarily blocked. The sacral roots, however, may be presumed to have been severely injured, requiring long periods for regeneration, if any is to occur. In case 2 the pain was due to a vascular disease of the legs, of which the mechanisms for pain are vaguely understood. Perhaps the pathways for pain in this case were scarcely touched. It is well to recall that Dogliotti expressed the belief that pain from vascular disease of the extremities does not respond to this method of treatment. Vesical disturbances are well known symptoms of lesion of the cauda equina. Bladder symptoms in hemicaudal lesion may be transient, but with the early appearance and persistence of incontinence one is to suspect a lesion of the conus. Since the sensory roots of from the first to the fourth sacral nerves carry the afferent fibers from the bladder, the hemicaudal nature of the lesions in the authors' cases, since they affected the bladder, is not contradicted by the apparent bilateral involvement of the fifth sacral root. Whether or not the tip of the conus medullaris was injured by the alcohol they are not prepared to say.

EDITOR'S ABSTRACT.

CHRONIC PROGRESSIVE (ENDOTOXIC) POLYNEURITIS. WILFRED HARRIS, Brain **58**:368, 1935.

Acute polyneuritis is one of the commonest diseases of the nervous system, but slowly progressive polyneuritis which is not due to any obvious cause, such as lead or alcohol, and in which the development of the symptoms is spread over many months, or even years, is as rare as the acute form is common.

Harris describes five such cases, in none of which a source of toxemia was discovered. Though varying in detail, the common features of slowly progressive

motor paralysis, with wasting and electrical changes and few sensory symptoms, are present in all cases. Recurrent attacks following short periods of complete recovery may or may not occur, and neural hypertrophy, too, may or may not be present. Two patients died as a result of respiratory failure and attacks of choking, which seems to be the characteristic ending in cases of the fatal progressive type.

The presence or absence of intermissions does not appear to be an essential feature distinguishing the recurrent form from chronic progressive polyneuritis. Such recurrences, in the absence of external toxins, would indicate a variation in the activity or development of an endotoxin rather than any essential difference between the recurrent and the steadily progressive form. Harris is of the opinion that an endotoxin or neurotoxin is the cause of the disease. In favor of this view he cites a case reported by Sorg (1897) and one by H. M. Thomas (1898), in both of which indigestion and abdominal pain were features of the illness before the development of the neuritis. In addition are three cases referred to by de Bruyn and Ruby Stern (1929), in which diarrhea was a prominent symptom.

The enlargement of the nerve trunks due to proliferation of the sheaths of Schwann and the interstitial tissue in certain cases of chronic progressive polyneuritis, does not appear important enough to justify separation as a distinct type of hypertrophic neuritis. The hypertrophic type described by Dejerine and Sottas (1893) is frequently juvenile and familial. It is slowly progressive for years, with talipes equinovarus and often kyphoscoliosis and usually severe pains, in association with peripheral anesthesia and much wasting. It often resembles the peroneal type of Charcot-Marie-Tooth atrophy and is always accompanied by posterior spinal sclerosis.

In conclusion, Harris suggests that all forms of recurrent or progressive neuritis as described in the paper, with the exception of Dejerine's familial type, whether or not associated with enlargement of the nerves, be grouped together as variations included under the term chronic progressive (endotoxic) polyneuritis.

SALL, Philadelphia.

CRURAL PARESIS ACCOMPANYING HERPES ZOSTER. G. P. CHANDLER, Lancet **1:** 1042 (May 4) 1935.

Chandler reports a case of herpes zoster in a man of 60. The eruption occurred in part of the distribution of the posterior root of the fifth lumbar nerve. It was accompanied by signs of involvement of the motor roots of the fourth and fifth lumbar and first sacral nerves. The patient complained of continuous severe pain in the right leg. Two days after the onset a herpetic rash appeared on the anterior aspect of the right knee and on the anterior and outer aspects of the upper third of the leg below the knee. Weakness of the right leg developed, and the right knee jerk was found to be absent and the right ankle jerk very sluggish. Pain disappeared one month after the onset, but there was some residual weakness. The knee and ankle jerks could be obtained only on reinforcement. It is Chandler's opinion that, if the modern view of herpes zoster is correct and myelitis of varying extent exists in every case, some degree of paresis of the muscles supplied by the affected segment may occur more frequently than is generally thought and that occasionally the major damage caused by the inflammatory reaction may fall on the cells of the anterior horn, causing paresis of the lower motor neuron type affecting muscles supplied by one or more segments of the cord. This may accompany a localized herpetic rash, as in this case.

WATTS, Washington, D. C.

A LOCAL EPIDEMIC OF NEURAXITIS. L. LE GUILLANT and P. LÔO, Ann. méd.-psychol. **93:**384, 1935.

In the years 1934-1935 Guillant and Lôo observed a peculiar epidemic in a large number of inmates of a neuropsychiatric institution. The condition was also observed in three patients outside the institution. The symptoms observed were

mainly disturbances of motility of all degrees up to complete flaccid paralyses, loss of deep reflexes and painful sensations in the extremities. The condition, which in some cases resulted in death but mostly in a certain degree of improvement, is considered to be a peculiar form of epidemic encephalitis, although it also has some of the characterisics of epidemic erythema. The fact that the condition was contracted almost exclusively by the inmates of a custodial institution, and among them especially those living under hygienically inadequate conditions, points to penury as at least a contributing factor in the development of the disease. This fact brings the disease in close relationship with the epidemic paralysis which is occasionally observed in hospitals for patients with mental disease. It also has a certain relationship to beriberi, pellagra and other diseases of malnutrition.

MOORE, Boston.

SYNDROME OF ADIE AND PERNICIOUS ANEMIA ASSOCIATED WITH POLYNEURITIC PSYCHOSIS: IMPROVEMENT UNDER TREATMENT WITH CASTLE'S METHOD. GEORGES PETIT and JACQUES DELMOND, Ann. méd.-psychol. (pt. 1) **94**:106 (Jan.) 1936.

Petit and Delmond report the case of a woman aged 56 who was not alcoholic and in whom in the course of about one year there appeared severe polyneuritis with psychosis characterized by disorientation in the three spheres, diffuse loss of memory, confabulations and an anxiety state, with delusions of interpretation. She had an advanced stage of pernicious anemia, paralysis of the lower extremities, with atrophy, muscular pain, loss of tendon reflexes, and the tonic pupils of Adie. The Wassermann reaction of the blood and spinal fluid was negative. On treatment with extracts of liver and stomach, combined with injections of sodium nucleinate, there occurred rapid improvement of both the physical and the mental condition. The blood picture became normal; muscular power returned, and she became able to walk; the tendon reflexes except the achilles and medioplantar returned, and the pupils became more alert in their reactions to light and in accommodation. The authors believe that infection with a neurotropic virus of the epidemic encephalomyelitic or neuraxitic type was the cause of the clinical picture in their case. They suggest that a disturbance of the tubero-infundibular nuclei caused by the infection could explain the triad of Korsakoff's syndrome, anemia and tonic pupils.

YAKOVLEV, Waltham, Mass.

TRANSITORY SYNDROME OF ADIE, ANEMIA AND ABORTIVE PARKINSONISM IN THE COURSE OF ACUTE MENTAL CONFUSION ASSOCIATED WITH LYMPHOCYTOSIS OF THE SPINAL FLUID. GEORGES PETIT and JACQUES DELMOND, Ann. méd.-psychol. (pt. 1) **94**:236 (Feb.) 1936.

Petit and Delmond report a case of tonic pupil associated with psychosis and anemia. The patient, a woman aged 48, showed at first changes of personality, and a few months later there developed acute psychosis, with confusion, hallucinations, delusions of influence, fuga and nocturnal incontinence. The spinal fluid showed 8 lymphocytes per cubic millimeter but no other abnormalities; the lymphocytosis disappeared a few weeks later. The urine contained sugar, acetone, albumin and urobilin. The Wassermann reactions of the blood and spinal fluid were always negative. The blood count was 3,300,000 red cells, with many neutrophilic myelocytes and 50 per cent polymorphonuclear and 47 per cent mononuclear leukocytes. All the tendon reflexes in the lower extremities were absent bilaterally. The pupils were irregular, the right larger than the left, and both reacted slowly to light and in accommodation. On treatment with liver, spleen and ovary, rapid improvement occurred, and the psychosis disappeared. The patient continued to show evidence of autonomic disturbance, tachycardia, painful palpitation and abnormal vasomotor reactions, and on two occasions a vesiculopustular eruption developed, which was radicular in its distribution. A few months later she began to show parkinsonian signs in the right arm—tremor and rigidity. The pupillary disturbances regressed, and the achilles reflex remained absent bilaterally. The authors

insist on a connection between Adie's syndrome and autonomic disturbances and abortive parkinsonism in the evolution of an acute confusional psychosis with anemia. They refer to several instances of this nature reported in the literature and discuss the hypothesis of a hypothalamic infectious origin of the psychic, hematologic, autonomic and pupillary symptoms. YAKOVLEV, Waltham, Mass.

COMPRESSION OF THE BRACHIAL PLEXUS BY THE NORMAL FIRST RIB. L. PUUSEPP, Folia neuropath. estoniana **11**:93, 1931.

A number of cases of compression of the brachial plexus by a normal first rib have been reported, and because the first rib was regarded as solely responsible for the compression its resection was advocated. However, Puusepp believes that the cause of the compression lies in a diminution of the triangle bounded by the scalenus anticus and medius muscles and the first rib by a variety of factors such as hypertrophy of the scalenus anticus muscle. Therapeutically, therefore, he aims at widening the triangle by cutting the scalenus anticus muscle and reports a case in which that has been done with recovery. This is to be preferred because of the greater risk involved in resection of the first rib.

N. MALAMUD, Ann Arbor, Mich.

Special Senses

CLINICAL CASES IN WHICH VERTIGO IS A CARDINAL SYMPTOM. JOHN B. MCMURRAY, Arch. Otolaryng. **22**:277 (Sept.) 1935.

In many cases of vertigo recovery has followed the removal of a suspected focus of infection. Other causes of vertigo have been hypothyroidism, obstruction of the eustachian tube, dental abscess, chronic infection of the tonsils, hyperthyroidism, cardiovascular disease and nicotine. One hundred and eighty-four cases of vertigo were studied. The frequency of vertigo was greatest between the ages of 35 and 55 years. About half the patients had normal hearing, and of these 80 per cent did not have constant tinnitus. The remainder of the patients had tinnitus most of the time. Forty per cent had bilateral nerve deafness, and 69 per cent with bilateral nerve deafness had no tinnitus. Ten per cent had unilateral nerve deafness, 20 per cent normal vestibular reactions, 53 per cent bilateral labyrinthine reactions, 53 per cent bilateral labyrinthine hypersensitivity, 5 per cent unilateral labyrinthine hypersensitivity; 10 per cent labyrinthine hyposensitivity, and 14 per cent a dead labyrinth. The caloric test was used in the examinations which McMurray made. Infection of the tonsils, teeth and prostate and chronic constipation were the most common conditions. In 104 of the 184 cases studied a diagnosis of toxic labyrinthitis was made. In 44 cases the central nervous system was observed to be involved. In 11 instances there was Ménière's disease. In the rest of the 184 cases the condition was not accounted for.

The conclusion is reached that foci of infection should be eliminated in cases of true vertigo. The author also concludes that if Ménière's disease is present and one does not know which ear is involved section of the vestibular nerve does not promise brilliant results. HUNTER, Philadelphia.

VISUAL DISORIENTATION IN HOMONYMOUS HALF-FIELDS. GEORGE RIDDOCH, Brain **58**:376, 1935.

By the term spatial orientation is meant the ability to localize objects seen in the three planes of space, especially to estimate absolute and relative distance. Defective spatial orientation in the visual fields as a result of bilateral cerebral lesion has been described by a number of observers, notably by Gordon Holmes. Sometimes stereoscopic vision has been lost, but this is exceptional.

In recorded cases of impairment of visual orientation the lesion, chiefly resulting from a war wound, was bilateral in the parietal lobe, so that the entire visual field

was involved, and, in addition, some limitation of the visual field for ordinary test objects complicated the clinical picture. Visual acuity was, as a rule, normal or nearly so.

The purpose in this report is to show that spatial disorientation may occur in homonymous half-fields alone as a result of unilateral lesion of the parietal lobe.

Riddoch reports two cases, in both of which tumor of the brain involving the left parietal lobe was presented. In the first case there was visual disorientation in the right homonymous half-fields, without loss of stereoscopic vision and with preservation of visual attention. The patient was able quickly to fix his gaze on an object and to maintain it to the left, but before operation less consistently to the right. Pupillary reactions and conjugate convergence were normal. Visual acuity was moderately reduced. The sole impairment of the visual field for ordinary test objects was enlargement of the blindspot in the left eye, due probably to secondary atrophy of the optic nerve. The patient was unaware of his visual disorder. In the second case there was visual disorientation in the right homonymous half-fields, with preservation of stereoscopic vision. Visual inattention in the right homonymous half-fields was at first present but disappeared about a fortnight after excision of the tumor. The patient could rapidly fix his eyes on a test object and follow it when moved. The pupillary reactions in accommodation and conjugate convergence were good. Visual acuity was slightly impaired. There was right homonymous hemianopia, at first incomplete and later complete, but two months after excision of the tumor the visual fields were full to small test objects. Visual disorientation persisted but was less marked than before. The patient was unaware of it.

These two cases show that visual disorientation in homonymous half-fields may result from lesion of the opposite parietal lobe. This defect may be dissociated from other more or less closely related disorders of visual function, which may follow a lesion of approximately the same part of the brain. Visual disorientation may be present without limitation of the visual fields for ordinary stimuli or serious disturbance of central vision.

In regard to the situation of the lesion, Holmes, on the basis of his cases of bilateral war wounds and of other recorded cases in which the lesion was also bilateral, concluded that visual disorientation results from lesions in the region of the supramarginal and angular gyri. In both the cases reported by Riddoch the tumor extensively invaded the parietal lobe, including the supramarginal and angular gyri. The ascending parietal convolution was little affected directly by the tumor, and the optic radiations had escaped.

As to the nature of the disturbance of function, little is to be added to the views already expressed by Holmes. Visual localization in the coronal plane depends largely on local sign of the retinal elements. Estimation of absolute and relative distance is, however, a much more complex function and is the result of the integration of immediate sensations and impressions from the retina, ocular muscles, labyrinth, neck and body and accumulated past experience. In other words, it is a function that is acquired by learning.

Visual disorientation may occur when the association pathways from the calcarine visual cortex to other parts of the brain are interrupted, and, so far as is at present known, the nodal point appears to be in the region of the supramarginal and angular gyri of the parietal lobe.

SALL, Philadelphia.

CAUSATION OF QUININE BLINDNESS. EUGENE WOLFE, Lancet **1**:1496 (June 29) 1935.

Wolfe states that two main views are still held with regard to the way in which quinine affects the visual apparatus. It is supposed (1) that it causes spasm of the retinal vessels and that the symptoms are due to the ischemia thus produced or (2) that it acts directly on the retinal elements, the spasm of the vessels being secondary to this. No adequate reason, however, is given for the spasm.

Wolfe states that quinine does not act as a vasoconstrictor on the tissues of the body generally and gives evidence to support this view. Binz believed that the action of quinine as a cell toxin was due to interference with oxidation and showed that the changes produced in lower organisms by quinine are similar to those produced by want of oxygen. Wolfe believes that quinine, in its capacity as a general protoplasmic poison, acts directly on the retinal elements. Spasm of the retinal vessels is secondary and is caused by extreme lack of oxygen. An ophthalmoscopic picture of greatly narrowed arteries and white disk, produced as an acute condition, much like that resulting from the taking of quinine, is seen after gastro-intestinal hemorrhage and after division or block of the arteria centralis. Loss of sight following hemorrhage is commonest after hemorrhage from a gastric ulcer. The hemoglobin content of the blood patients with gastric ulcer is usually low and falls steadily for several days after a hemorrhage. The onset of blindness is often accompanied by giddiness, faintness and loss of consciousness, which are themselves symptoms of general lack of oxygen. Regarding spasm following block of the arteria centralis, Uhthoff found that when he put a clamp on the optic nerve behind the globe there was a latent period of from five to ten seconds before the retinal vessels went into spasm. The same latent period was noted when he divided the nerve. This seems to indicate that the spasm is produced not by cutting off the blood current directly but by the lack of oxygen in the retina.

The common factor in blindness in quinine poisoning, hemorrhage and block of the arteria centralis is extreme lack of oxygen.

WATTS, Washington, D. C.

DISORDERS OF OCULAR MOTILITY ASSOCIATED WITH INCOMPLETE DEVELOPMENT OF THE GENITAL SYSTEM. N. LAMBROULIAS, Ann. d'ocul. **172**:790 (Sept.) 1935.

Lambroulias reports the case of a boy aged 14 who had exophoria and periodic homonymous diplopia, associated with insufficient development of the pelvis and testes. The patient's condition improved after opotherapy. BERENS, New York.

CONGENITAL ABSENCE OF ABDUCTION WITH ENOPHTHALMOS OCCURRING DURING ADDUCTION. I. NICOLACOPOULAS, Ann. d'ocul. **172**:796 (Sept.) 1935.

Nicolacopoulas describes a case in which there was complete congenital absence of abduction of the left eye, associated with diminished adduction. This was accompanied by enophthalmos of 2 mm., diminution in the size of the palpebral fissure and slight rotation of the eyeball downward. BERENS, New York.

ANGIOSCOTOMA AND CHRYSALBINE. A. L. DUBOIS, Ann. d'ocul. **172**:945 (Nov.) 1935.

According to Dubois, in six cases of chrysalbine poisoning certain functional disturbances were presented, which consisted of blurred vision and seeing rainbows, rainbow circles and halos. Ophthalmoscopically these disturbances could not be associated with objective lesions. However, angioscotometry showed the presence of large scotomas extending into the blindspot of Mariotte and surrounding the point of fixation. The amount of chrysalbine administered did not affect the appearance of symptoms. BERENS, New York.

SCOTOMA IN ACUTE RETROBULBAR NEURITIS. L. GENET, Ann. d'ocul. **173**:133 (Feb.) 1936.

Genet calls attention to the rapid improvement of so-called acute retrobulbar neuritis by means of nasal treatment. He also mentions that the position of the scotoma may change rapidly. These changes in the position of the scotoma and the rapidity of the improvement in vision in certain cases cause one to question

whether these symptoms are caused by neuritis in the strict sense of the word or whether they are only vascular disturbances producing angioscotoma. The latter interpretation permits the better understanding of the rapid improvement which occurs in this condition after nasal intervention, for in these cases operation on the trigeminal group of sympathetic nerves may cause a reflex which favorably influences the circulation in the optic nerve

BERENS, New York.

DISTURBANCES OF FUNCTION OF THE VERTICAL SEMICIRCULAR CANALS IN TWO CASES OF PARALYSIS OF FUNCTION OF THE OCULAR GLOBES: DISSOCIATED AUTOMATICOREFLEX PARALYSIS OF THE VESTIBULAR TYPE. G. E. JAYLE, J. ALLIEZ and J. PAILLAS, Rev. d'oto-neuro-opht. **13**:603 (Sept.-Oct.) 1935.

On the basis of two cases occurring in their own experience and the observations of other investigators, Jayle, Alliez and Paillas discuss the question of vestibular reflectivity. In a case of multiple sclerosis there was paralysis of movements of the globe to the right and left. Caloric and rotation tests in various positions of the head produced no nystagmus. In a case of parkinsonism following epidemic encephalitis, excursions of the globe to the left and downward were diminished. Spontaneous horizontal nystagmus to the left and right was present. Stimulation by rotation produced no rotatory nystagmus, no vertical nystagmus upward and perverted nystagmus in the left eye in the test which normally should produce vertical nystagmus downward. Aubry and Caussé have observed abolition of provoked rotatory nystagmus in cases of Friedreich's disease, multiple sclerosis, anterior cerebellar tumor and tumor of the cerebellopontile angle. Blum reported three cases of encephalitis in which provoked rotatory nystagmus was abolished, and Jonesco-Sisesti mentioned the same phenomenon in a case of syringobulbia. The authors believe that to the two classic types of paralysis of function of the ocular globes must be added dissociated automaticoreflex paralysis of vestibular type. The only conclusion to be drawn from these observations is that there exist different anatomic pathways for each of the functions envisaged, but there should be no haste in adopting this conclusion because too much about ocular motility remains unknown.

DENNIS, San Diego, Calif.

TWO CASES OF HEREDITARY NYSTAGMUS. R. CAUSSÉ and A. MARTIN, Rev. d'oto-neuro-opht. **14**:86 (Feb.) 1936.

While much has been written about vestibular nystagmus, the literature of congenital nystagmus is meager, and much obscurity of its pathogenesis remains. Caussé and Martin discuss only two points, brought out by the study of two cases of congenital nystagmus in brothers: the familial and hereditary character of the disease and the replacement of the spontaneous nystagmus by an inverted optokinetic nystagmus. The hereditary and familial character of the disease is exemplified by the fact that it was present in three brothers and one first cousin; only males were affected; it existed in only one generation, and research revealed that three of the antecedents had mental disturbances, two diabetes and one marked myopia. Other defects were also found, but no case of albinism was discovered.

Bárány first described inversion of optokinetic nystagmus, and others have demonstrated that it occurs only in association with optic or congenital nystagmus, never with spontaneous vestibular nystagmus; the phenomenon is not constant. In the cases described it was difficult to replace the nystagmus with optokinetic nystagmus, and, even when this occurred, the inversion could not be obtained in the four fundamental directions—upward, downward, to the right and to the left—but occurred in only one or two directions, which were always the same. The direction of the inversion seemed to correspond to the direction of the spontaneous nystagmus that was most active.

DENNIS, San Diego, Calif.

INEQUALITY OF THE PUPILS ARISING FROM THE SYNDROME OF SYMPATHETIC STIMULATION. A. TOURNAY and G. FOURQUIER, Rev. d'oto-neuro-opht. **14**:186 (March) 1936.

Studies were made of the pupillary reactions of two patients, one with excitation and another with paresis of the sympathetic nerve supply. The pupils were examined with just enough light to enable one to see the pupil; then the illumination was greatly increased and, last, the lighting was suddenly dimmed. Inequality of the pupils was noted in each degree of illumination. In the first patient the dilated pupil was on the side of the irritation, and, in addition, it was observed that the abnormal pupil dilated again more rapidly than the normal pupil when the lighting was diminished. In the other patient, in whom there was a deficit of sympathetic innervation due to injury, resulting in contraction of the pupil, the second dilatation of the affected pupil was slower than that of the other pupil. These phenomena were confirmed by flash-light photographs, and the size of the pupils was measured directly from the plates. DENNIS, San Diego, Calif.

THE LOCALIZATION OF THE MACULAR FIBERS IN THE OPTIC RADIATIONS. ADOLPH JUBA, Ztschr. f. d. ges. Neurol. u. Psychiat. **153**:123 (Oct.) 1935.

Juba reports the results of a careful anatomic study of the brain of a woman aged 84 in which a circumscribed softening was observed in the cortex of the right occipital pole. There was little involvement of the white matter. Degeneration of ganglion cells was observed in the most caudal portion of the right external geniculate body. This area was wedge-shaped, with the apex directed ventrally. The left external geniculate body was intact. The picture was that of retrograde degeneration. The tapetum and the stratum sagittale internum on the right side showed marked demyelinization, especially in their ventral portions. The vertical limb of the optic radiations was involved. The lower or ventral one third to one fourth of the vertical limb of the stratum sagittale externum was also demyelinated.

The observations in this case confirm the results of previous investigators, who observed that the most caudal part of the external geniculate body is the end-station for the primary neurons of the macular bundle. The occasional intact islets of parenchyma in this degenerated part of the external geniculate body could be explained by the sparing of some of the cortical tissue in the softened area of the right occipital lobe. This anatomic study corroborates the contentions of Poljak and others that a point for point projection exists between the occipital cortex and the external geniculate body. Weigert preparations in this case indicate the probability that the macular fibers run through the ventral part of the vertical limb of the optic radiations. The absence of any alterations in the left external geniculate body is evidence against the theory of bilateral cortical representation of the macular. Juba admits, however, that a final conclusion regarding this point cannot be made on the basis of data such as are presented in this case.

SAVITSKY, New York.

Society Transactions

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, Nov. 21, 1935

D. M. Olkon, M.D., *Vice President, in the Chair*

Antigenic Properties of Tumors of the Brain. Dr. Arthur Weil and Dr. Erich Liebert.

An attempt was made to produce antiserums against aqueous emulsions and alcoholic extracts of different types of glioma by injecting them intraperitoneally into guinea-pigs. It was demonstrated that alcoholic extracts of gliomatous tissue fixed in formaldehyde and injected into guinea-pigs in combination with dog's serum produce antiserums. These antiserums against alcoholic extracts of gliomas are more specific than antiserums against aqueous emulsions of the same tumors. It was not possible to differentiate a glioblastoma and a medulloblastoma by means of the complement fixation test by using an antiserum against an aqueous emulsion

Degree of Complement Fixation

Injected Alcoholic Extracts or Aqueous Emulsions	Alcoholic Extracts as Antigen				
	Glio-blastoma I	Glio-blastoma II	Medullo-blastoma	Scar Tissue	Human Brain
Glioblastoma I aqueous emulsion.....	11	9	10	5	5
Glioblastoma I alcoholic extracts.....	6	9	3	3	6
Glioblastoma II aqueous emulsion.....	9	7	10	9	6
Glioblastoma II alcoholic extract.....	7	8	4	2	1
Medulloblastoma aqueous emulsion.....	5	6	12	8	5
Medulloblastoma alcoholic extract.....	6	5	10	4	6
Scar tissue aqueous emulsion.....	11	11	9	15	4
Human brain aqueous emulsion.....	3	6	1	6	11
Human brain alcoholic extract.....	5	4	3	5	12

of glioblastoma and the alcoholic extracts of the tumor as antigen. When, however, antiserums against alcoholic extracts of tumor (plus serum) were used, the differentiation between glioblastoma, medulloblastoma, brain tissue, astrocytoma and scar tissue from organized hemorrhagic softening was possible.

In the accompanying table, which presents a summary of the different experiments, the figures indicate the sum total of the different degrees of complement fixation in a series of 5 test tubes for each antigen in dilutions ranging from 1:6 to 1:50. The different degrees of complement fixation are expressed by figures, such as 4 for no hemolysis and 0 for complete hemolysis.

It was attempted also to demonstrate the formation of antibodies in the serum of patients with glioma. For a preliminary experiment, the serums of 2 patients with verified glioblastoma were tested. The first patient had been operated on approximately six weeks before and had since been treated with roentgen rays. The serum of the second patient was obtained before the operation and also three days after. The serum of the first patient contained amboceptors against alcoholic extracts of glioblastoma, medulloblastoma and human brain as antigens but did not bind the complement in combination with alcoholic extracts of the kidneys and heart and of carcinoma, while that of the second patient contained no amboceptors against any of these antigens either before or after the operation.

MENINGO-ENCEPHALOMYELITIS NEONATORUM: PATHOLOGIC REPORT OF A CASE. DR. RICHARD B. RICHTER.

An infant, aged 7 weeks, died in a convulsive state after an acute illness of only a few days. There was moderate anemia. The spinal fluid was xanthochromic, contained 33 cells and gave an unsatisfactory reaction to the Wassermann test. The Wassermann test of the blood was not made. In roentgenograms of the long bones there were fine lines of increased density about 5 mm. back of the epiphyses. These changes were not characteristic of syphilis.

Autopsy showed the brain to be normally developed but to contain extensive areas of softening and necrosis, many of them presenting grossly the appearance of caseation from the deposit of huge quantities of calcium soaps. These regions involved the central gray matter, the cortex and the white matter indiscriminately and impinged on both the ventricular and the pial surfaces. Microscopically, the necroses presented as a homogeneous colloid change, in great part calcified. In and about these regions was an intense cellular reaction consisting of fat granule cells, hyperplastic glia cells, proliferating fibroblasts and rod cells and enormous numbers of plasma cells. The plasma cells were present not only in the adventitial spaces of the vessels but in large aggregations free in the tissues. There were striking proliferation of new capillaries and generalized thickening of medium-sized blood vessels. A widespread leptomeningitis was present, both cerebral and spinal, in which the exudative elements were chiefly macrophages and plasma cells. Much fibroblastic proliferation had occurred in the meninges, and there was a marked tendency toward organization of superficial cortical lesions by meningeal fibroblasts. At one level of the spinal cord a destructive inflammatory focus was found which presented the same essential features as those in the brain. No changes suggestive of syphilis were found in any of the organs, including the liver, or in the bones. Numerous attempts to stain spirochetes by all of the usual methods yielded negative results.

The case is presented as an example of inflammatory encephalitis of nonsyphilitic origin in the brain of a new-born infant. The process was perhaps congenital. Such examples are rare in the literature, and it is urged that such terms as encephalitis congenita, encephalitis neonatorum, etc., be reserved for conditions of this type presenting the pathologic credentials of a true primary inflammation.

DISCUSSION

DR. PAUL C. BUCY: I should like to ask Dr. Richter if he has considered the possibility that this patient's condition may be lead encephalopathy. The resemblance of the condition to that in cases of lead encephalopathy which have been reported is striking, particularly the presence of lines of increased density at the ends of the shafts of the long bones, as seen in the roentgenograms.

DR. D. M. OLKON: Were roentgenograms taken of the long bones in Dr. Richter's case? The presence of opaque bands at the epiphysial ends of the long bones is considered good evidence of deposit of lead.

DR. RICHARD B. RICHTER: I am much interested in Dr. Bucy's suggestion. I had not seriously thought of lead encephalopathy in connection with this case, but as presented by Dr. Bucy the idea sounds attractive and reasonable. The child died shortly after admisssion to the hospital, and it has not been possible to locate the parents to learn anything more about the history.

NOTE: Subsequent to this discussion the brain was analyzed for lead content and was found to contain 0.427 mg. of lead in 200 Gm. of brain tissue, as compared with 0.335 mg. of lead in the same amount of tissue of a control brain from a child of the same age. The difference was not considered significant.

TREATMENT OF DEMENTIA PRAECOX WITH SULFUR IN OIL. DR. CHARLES F. READ and DR. LOUIS B. SHAPIRO.

The mental disorder known in state hospitals as dementia praecox demands treatment despite present ignorance as to its etiology and pathology. A review

of the literature indicates that the great majority of those who have reported concerning treatment with sulfur believe that it is decidedly helpful. We find that good remissions occur only in cases of recent involvement but that amelioration, often temporary to be sure, occurs even in cases in which the condition is chronic.

Investigation of a group of patients with dementia praecox, taken in the order of their admission during 1930 and before treatment with sulfur in oil came into use, revealed fewer favorable results. This in itself is not conclusive evidence that the remissions we report were actually caused by sulfur in oil. However, as the patients showed a definite change in the mental condition soon after the institution of treatment, it seems fair to assume that at least the duration of the acute psychosis was shortened.

In a considerable number of patients with dementia praecox of short duration showing confusion, perplexity and indecision or periods of excitement alternating with periods of stupor, rapid deterioration took place. It is our impression that this treatment has prevented such an unhappy outcome in a number of our patients.

We are convinced of its value in the care and treatment of patients with chronic dementia praecox who show excitement, destructive and combative tendencies and filthy behavior, in whom any amelioration of obnoxious symptoms is gratifying. A marked decrease in the number of injuries in our services devoted to persons with acute dementia praecox has occurred since this treatment has been instituted.

We are not in a position to voice an opinion concerning the modus operandi. The literature seems to show that sulfur administered parenterally does not remain inert, but we think that to a certain extent the benefits derived from the treatment, in some cases a least, are ascribable to psychogenic factors. Discomfort at the site of injection serves as a focus for reorientation of the patient's interest in the direction of reality. Several have remarked spontaneously that they became better because the discomfort in the legs served as something real to which they could fasten their attention.

Conclusions.—1. A review has been made of the literature, with a compilation of the results obtained in 575 cases of dementia praecox in which sulfur therapy was used.

2. Laboratory studies in 19 cases have shown a decided rise in blood sugar values in 10 cases and no special change in the remainder.

3. A constant drop in the values for the cholesterol content of the blood occurred in all but 1 case during treatment.

4. Leukocytosis ranging between 10,000 and 20,000 was a constant feature.

5. Of 176 patients treated at the Elgin State Hospital, 13 have shown remissions and 55 an amelioration of symptoms. A corresponding number of patients with dementia praecox chosen at random—176 admitted consecutively before sulfur was used—did not evidence such good results.

6. The results obtained may be due to the therapeutic activity of the injected sulfur, to a nonspecific fever reaction or to an improved orientation to reality. Possibly all three factors are concerned.

DISCUSSION

DR. LOUIS B. SHAPIRO: I wish to stress a few points in regard to this presentation. First, the subtitle of our paper is "therapeutic impressions." Second, I am anticipating the objection that many of these patients might have recovered even if nothing had been done except putting them to bed and giving more attention; however, I think that the improvement, beginning soon after the treatment was instituted or within two or three weeks after treatment, at least points to shortening of the period of acute psychosis. It may be that many of these patients would have deteriorated markedly without showing any improvement. Many of the patients with chronic dementia praecox who suffered from periods of acute excitement were also benefited by what we call an amelioration of symptoms. They became less combative and less irritable, as a result of the treatment I think, and

showed marked improvement. I should say that this form of treatment has been beneficial in shortening the acute phase of the psychosis and in shortening the periods of excitement occurring in the chronic stage.

DR. ALFRED P. SOLOMON: Although this paper offers valuable considerations from a therapeutic standpoint, I think that there is a possibility of studies of this kind being of even greater value in that they afford an opportunity for one to divide those cases of dementia praecox in which there is a tendency to improvement or recovery with this type of treatment from those on which there is no improvement. The latter approach is predicated on the more or less generally accepted assumption that within the categorical subgroups there are a number of distinctly different types which differ in genesis and psychologic structure.

I was particularly interested in Dr. Read and Dr. Shapiro's comment that the majority of those persons who recovered had dementia praecox of the catatonic type. In studies on this subject by means of continuous records of the reaction of the skin to the galvanic current and the blood pressure, Dr. Chester Darrow and I have found it convenient to separate the patients with dementia praecox into those who are actively and those who are passively withdrawn; we find that physiologically they are distinctly different. It is in the group of actively withdrawn persons, which includes those who are catatonic in their clinical behavior, that I should anticipate recovery with treatments such as those outlined by Dr. Read and Dr. Shapiro. These patients are in contact with the outer world; they resist feeding by closing lips and teeth tightly; they are mute unless angered or caught by surprise, giving the impression that they will not talk; they push away the nurses and actively resist passive motion or activity of any kind.

DR. CLARENCE A. NEYMANN: As early as 1906 Lundval injected into certain persons with dementia praecox a solution consisting of cinnamic acid, sodium cinnamate and the sodium salt of nucleic acid. I have forgotten the exact proportions. This solution will increase the number of white cells and the temperature will rise to about 103 F. In 1916, while I was a member of the Henry Phipps Psychiatric Clinic of the Johns Hopkins Hospital, we treated about 10 patients with this solution and obtained results that were comparable to those obtained by Dr. Read and Dr. Shapiro. There, too, the action seemed to depend more on the psychic effect than on anything else. The patients who were especially affected and therefore benefited were of the type that were withdrawn and introverted, the simple or hebephrenic schizophrenic type, and it seemed that the pain and discomfort combined with the hyperpyrexia drew their attention to themselves and forced them to resume contact with reality. This work, I believe, was somewhat analogous to that presented here. It is of interest to note that if the schizophrenic patient is treated with hyperpyrexia alone, such as may be produced by diathermy, radiothermy or electromagnetic induction, he does not seem to respond with a greater development of interest in the surroundings. The response, or return to reality, is short and coincides with the day on which treatment is to be given. Therefore, I believe that the pain of the injection has a decided bearing on the change in mental attitude. It is well known that injections of sulfur in oil are painful. I did not gain a clear comprehension as to what group of patients was most benefited, those with the catatonic, the excited, the stuporous, the withdrawn or the paranoid type. It was our impression that those with the paranoid type did not respond to treatment with the solution used by Lundval and, if anything, showed more pronounced paranoid trends after the injections.

DR. FRANCIS J. GERTY: The outcome of treatment of dementia praecox is discouraging. Not only is the prognosis poor, but when the patient does improve markedly or recover one does not know why. Many forms of treatment have been suggested—eradication of focal infection, resection of the colon, trephination of the skull, injection of foreign proteins, electropyrexia, injection of sulfur in oil, reeducation, etc., and with each there have been reports of improvement and recovery. I think that progress might be made in the treatment for dementia praecox if the few cases in which the patient seems to have recovered and those

in which there has been marked improvement were selected and studied intensely. I believe that method lay behind the discovery of the value of fever therapy for dementia paralytica.

Another point that has been raised here is that of the psychogenic origin of some of the results. Possibly there is something to psychogenic improvement, for all of the various types of treatments are reported to bring about improvement.

DR. CHARLES F. READ: As I see it, practically all of the discussion has been anticipated to a certain extent in the paper as presented. For example, none would deny the apparent psychogenesis in many of our cases. What lies behind this break in adjustment has not been decided. I shall not attempt to answer each speaker in order, but as to the types affected by this treatment I should say, first, that we have not dealt with patients with paranoia except when their condition was acute and there was a history of paranoid ideas early in the disease. We have treated some hebephrenic patients and temporary but very brief amelioration has occurred. Most of the patients showed stupor, confusion, etc., the acute picture which may be diagnosed as catatonia or as "indeterminate," as it often is in staff meetings at the Elgin State Hospital. These patients with acute dementia praecox have been especially benefited. In the chart it was shown that in the 176 cases, as compared with the problematic control group, there were 13 remissions as against 3.

We mentioned Dr. Lundval's treatment which I tried out a number of years ago, with some good results. One man with catatonic dementia praecox was climbing the screens on the porches in his excitement. The day after treatment was instituted the nurses asked what we had done for this man, who had become tractable and reasonable within forty-eight hours. He was dismissed and after a time married; years afterward he returned with another attack of a catatonic character. The remission may last for a few weeks or for many months and then treatment may be reinstated. We sometimes give two or three courses. We do not claim that sulfur in oil is a specific. That would be foolish.

I agree with Dr. Gerty that one should inquire carefully into all the possible causes for remissions in patients who seem to recover "spontaneously." With smaller groups and closer observation one might determine in what manner these remissions have been precipitated.

POSTURAL REACTIONS FROM STIMULATION OF THE INTERIOR OF THE CEREBELLUM. DR. H. W. MAGOUN and DR. W. K. HARE (by invitation).

The excitability of the interior of the cerebellum of normal monkeys and of normal and decerebrated cats was demonstrated by electrical stimulation. Access to the cerebellar nuclei and the adjacent fiber paths was attained by the use of a needle-like bipolar electrode, the position of which in the interior of the brain was controlled by the Horsley-Clarke stereotaxic instrument. A weak faradic current was led from the secondary coil of a Harvard inductorium. The exposed tips of the otherwise insulated electrodes were 1 mm. apart. For observation, the animals, lightly anesthetized with pentobarbital sodium, were suspended by strings passing under the supraspinous ligament so that the head, trunk and extremities were freely movable. The responses of the animal to excitation of the cerebellum were most carefully distinguished from control responses to activation of the cranial nerves or the medulla. The latter were jerky, clonic and limited to the period of electrical stimulation, and there was only relaxation after stimulus. Stimulation in the cerebellum, on the other hand, was followed by a rebound posture that was maintained for as long as from five to ten minutes, during which time it slowly relaxed. A second stimulus at any time during this rebound produced either an inhibition of this posture or a contraction of the antagonists of the muscles active during the rebound. This phase lasted only as long as the period of stimulus, and when it was concluded the rebound posture was immediately resumed.

Stimulation of the cerebellum initiated three distinct types of response:

1. The first type involved the eyes, head, trunk and tail and all four limbs. During the first phase either there was an inhibition of any preexisting muscular contraction, or the eyes, head, concavity of the body and the tail were directed toward the side on which the point of stimulation was located. The ipsilateral limbs were flexed and the contralateral limbs extended. The instant the electrical current was stopped this posture gave way to an opposite posture, the rebound. The concavity of the entire vertebral column was directed to the side opposite the point in the cerebellum which had been stimulated. The ipsilateral limbs were fully and rigidly extended; the contralateral limbs were strongly flexed. Reactions of this nature were obtained from the base of the folia of the vermis, from the underlying white matter and from the fastigial and globose nuclei.

2. Reactions from the emboliform nucleus and the overlying white matter were generally confined to the ipsilateral forelimb. During stimulation the limb was relaxed, and on rebound it was flexed.

3. Scratching and grasping, usually with only the ipsilateral forelimb, occurred during the first, or stimulatory, phase. The rostral end of the cerebellar nuclei and the vicinity of the superior cerebellar peduncle are the only regions which yield this response. Only in the monkey was the third type of reaction observed.

The efferent paths were not established for any of these responses beyond the fact that the brachium conjunctivum is not essential for the first two types of response. These could be obtained in the cat when the level of decerebration was caudal to the red nuclei.

Some general features of the first type of response were further investigated in the cat. The rôle of tonic reflexes in the prolonged maintenance of these rebound postures was studied by observing the duration of rebound contraction after the elimination of tonic labyrinthine and myotatic reflexes.

These observations were made on a deafferented forelimb after fixation of the neck in the midline, denervation of the opposite forelimb and elimination of the hindlimbs by section of the lower part of the thoracic portion of the spinal cord. In 6 of the 13 animals used bilateral labyrinthectomy was also performed.

It was found that the duration of the prolonged rebound contraction which follows stimulation of the cerebellum in the normal animal was considerably reduced by deafferentation of the limbs and appeared to be decreased a little more by labyrinthectomy in addition to deafferentation. But after the elimination of all of the afferent impulses on which the tonic effects of the stretch and labyrinthine reflexes depend, continued discharge of both flexor and extensor centers for the forelimb was observed for periods varying from a few seconds up to a minute or longer.

In normal animals a number of control experiments were performed on cerebellar "release" effects, these effects being produced by extirpation of the cerebellum, by excessive puncturing of the cerebellum with the needle electrodes, by undercutting the medial cerebellar nuclei or by the injection of solution of cocaine into the medial portion of the interior of the cerebellum, the latter method eliminating any possible irritative factors. The only consistent effect observed as a release from one half of the cerebellum was an extensor rigidity of the ipsilateral forelimb, which falls far short of duplicating a typical rebound posture. The "release" effects obtained after hemidecerebellation differed also from the rebound posture observed after cerebellar stimulation in that the former (1) persisted indefinitely and (2) could not be reversed in the rebound posture after stimulation of the opposite half of the cerebellum.

Finally, the problem of the identity of the inhibition produced by stimulation of the cerebellum and that elicited by stimulation of the cerebral cortex was studied. In 4 normal animals under light anesthesia with pentobarbital sodium, the effect of stimulation of the region of the sigmoid gyri of the cerebellar cortex on cerebellar rebound extension was observed before and after section of the pyramids, the

inhibition obtained from stimulation of the cerebellum being used as a standard of judgment for cerebral effects.

Before section of the pyramids, stimulation of either cerebral cortex produced an inhibition of the rebound extensor posture of the forelimb contralateral to it, usually but not invariably in conjunction with active flexor movements, and in two animals less regular ipsilateral inhibitory effects were observed. After section of the pyramids, stimulation of either half of the cerebral cortex was without effect on the extensor posture of either forelimb, although stimulation of the cerebellum produced as regular an inhibition of the rebound extensor posture as before.

These experiments demonstrate a cerebral inhibition capable of acting on the rebound extension after stimulation of the cerebellum over a pyramidal pathway for at least as far caudad as the upper part of the medulla. They give no evidence of an extrapyramidal cortical inhibitory influence acting through the cerebellum. The results complement the recent findings of Rioch and Rosenblueth, of which we were unaware when our experiments were completed, which demonstrate that cerebral inhibitory effects are unimpaired after complete extirpation of the cerebellum.

DISCUSSION

DR. PERCIVAL BAILEY: I do not see, arguing anatomically, why the cortex should have so much influence on these reactions, as they are obtained from the nuclei of the roof. The connections of these nuclei being largely from the spinal cord via the vermis and having little to do with the cortex, I should expect that the cortex would have little influence. I know the different parts of the cerebellum have been poorly understood, but I should like to have the authors explain how the cortex anatomically might influence these reactions.

DR. R. W. GERARD: I wish to congratulate the authors on an extremely well controlled study of a difficult problem.

The question I wish to raise is a step beyond their analysis and is in no sense a criticism of what they have done. The work eliminates the possibility of a reflex origin for the prolonged postural rebound. I wonder, however, if they can properly refer to the maintained motor effect as "after-discharge," as it is the reverse of the discharge obtained during stimulation. Was the strength of stimulation varied over any wide range to see if the two effects, inhibition and later contraction of muscle groups, are to any extent separable? Also, what does strychnine do? I am thinking of the old experiments of Sherrington on different afferent fibers in a mixed nerve, some giving the prompt inhibition and others the rebound "after-discharge."

DR. H. W. MAGOUN: In answer to Dr. Bailey, we did not expect the cerebral cortex to influence these postures through a cerebellar pathway, but that view has been advanced by other workers, notably Weed and Wärner and Olmstead. Our experiments were performed to see if we could demonstrate a cerebral inhibition acting through the cerebellum, and we have not been able to do so. The work of Bremer should be recalled in this connection. Bremer found cerebellar inhibition to be well developed in the pigeon, in which the cerebral cortex is rudimentary and the corticopontocerebellar system entirely lacking.

I thank Dr. Gerard for his comments. We have not gone beyond the observations that have been reported. We realize that the description of these rebound effects as "after-discharge" is not in keeping with the common definition of "after-discharge" as referring to the prolongation of the same effect obtained during stimulation. If electrical stimulation of the cerebellum activates the mechanism responsible for these rebounds, as it must do in some way, this mechanism is not able to manifest itself until stimulation has ceased. Then the rebound effect, whatever its mechanism may be, comes into play and is continued far beyond the time for which the brief stimulation could be directly responsible. It seems to us that some mechanism of prolonged central excitement must underlie the maintenance of these rebound postures, and it may be recalled that in explanation of just such activity closed reverberating or self-reexciting neuron circuits have been postulated by Ranson and Hinsey and by Lorente de Nó.

Regular Meeting, Dec. 19, 1935

D. M. Olkon, M.D., *Vice President, in the Chair*

Acute Epidural Spinal Abscess: A Clinical Entity. Dr. Benjamin M. Gasul and Dr. Richard H. Jaffé (by invitation).

Three patients with acute epidural spinal abscess came under observation in five months, and the cases are deemed worthy of report.

Case 1.—A blister appeared on the right knee of a boy, aged 8 years, and was treated with mercurochrome. On the next day pus was discharged from the wound, and there was slight fever. In the next few days the fever had increased, and there were restlessness, abdominal distention, vomiting, pain and stiffness in the back and soreness of the neck.

On examination one week after the onset (February 22) a sore was still present on the knee. There were also hyperesthesia of the lower extremities, a diminished knee jerk bilaterally and positive Kernig and Brudzinski signs. The leukocyte count was 18,000, with 97 per cent polymorphonuclears. Spinal puncture revealed diminished pressure, and the fluid contained 10 lymphocytes. Cultures of material from the wound revealed Staphylococcus aureus nonhaemolyticus. On February 23 the spinal fluid was blood tinged and purulent; it contained gram-positive cocci. The cisternal fluid was under increased pressure and contained 110 cells, most of which were lymphocytes. On February 24 a metastatic abscess appeared on the dorsum of the left foot; on this day also cultures of the blood and of the cisternal fluid yielded the staphylococcus.

Laminectomy on February 24 revealed an extradural abscess beneath the laminae of the second and third lumbar vertebrae. In spite of the appearance of other metastatic abscesses the patient gradually improved, and by May 24 he was well.

Case 2.—A girl, aged 13 years, experienced attacks of severe radiating pain in the left side of the chest, which occurred several times a day and lasted about an hour. The attacks became progressively more frequent and severe. On April 7, 1934, two and a half weeks after the onset, weakness and a "sleepy" feeling appeared in the left leg and were followed by paralysis; the right leg was similarly affected the next day, and there appeared also incontinence of feces and dribbling of urine. On examination on April 11 there was complete flaccid paralysis of the legs and abdominal muscles, with complete loss of reflexes and total anesthesia below a line midway between the xiphoid process and the umbilicus. An area of tenderness was present over the sixth and seventh dorsal vertebrae. Spinal puncture revealed clear fluid under diminished pressure, with 5 lymphocytes per cubic millimeter. The test for globulin gave a positive reaction, and the total protein content was 76 mg. per hundred cubic centimeters. The leukocytes of the blood numbered 20,300, with 86 per cent polymorphonuclears.

Laminectomy was performed on April 11. Pus was present in the muscles overlying the left side of the fifth and sixth thoracic vertebrae, and similar yellow pus was observed beneath the lamina of the sixth vertebra. Because of the advance of the infection above the level of anesthesia, the wound was reopened on April 14, and another pocket of pus was observed beneath the fifth lamina. Fever of a septic type continued for several days, but the patient's condition gradually improved. Three months later she was well, though the neurologic findings remained unchanged.

Case 3.—A boy, aged 3 years, became ill with fever, cough and sore throat on July 16, 1934. When he was examined at the Cook County Hospital on July 23 the temperature was 105 F.; the tonsils were enlarged, and the Kernig and Brudzinski signs were positive. Lumbar puncture revealed purulent fluid containing many cocci. Treatment for epidemic meningitis was instituted. Cisternal puncture revealed fluid that was only slightly opalescent, with 100 cells and no micro-organisms. The leukocytes of the blood numbered 13,200.

On July 24 laminectomy of the third, fourth and fifth lumbar vertebrae revealed pus opposite the fifth vertebra and recent purulent pachymeningitis. The child's temperature rose to 108.8 F., and he died on the same day.

Autopsy revealed suppurative peripachymeningitis, which extended from the surgical wound to the upper part of the cervical region. The inner surface of the dura was injected and cloudy, and the leptomeninges were separated by an increased amount of cloudy fluid. There was a small abscess in the left tonsil.

DISCUSSION

DR. G. B. HASSIN: The clinical diagnosis of epidural spinal abscess is not difficult if slowly progressive spastic paraplegia, with disturbances in sensation and bladder control, develops in the presence of infection. At one time it was thought that epidural abscesses are usually, if not exclusively, due to osteomyelitis of the vertebrae, but they may occur from any infection. It is possible to show that the spastic paraplegia and sensory disturbances are not due to so-called pressure on the cord. The lantern-slides I present, for instance, show distinctly that the spinal epidural abscess exerted no direct pressure on the cord, as it was divided from the latter by a thickened dura, a wide subarachnoid space and a hyperplastic pia. The spinal cord, however, exhibited marked changes in the form of rarefied areas or stasis. The changes should not be classified as pressure myelitis.

DR. PETER BASSOE: This paper gives a clear picture of this disease. It shows how well this disorder is now understood in this community. This is in marked contrast to the situation at a meeting about fifteen years ago, when this subject was presented, I think for the first time, by Dr. E. W. Ryerson and me. We demonstrated a woman, aged about 20, who had been taken ill suddenly with severe pain in the midthoracic region. For a week she had high fever and a high degree of leukocytosis, and then paraplegia set in. A neurologist had seen the patient, and the first diagnosis was poliomyelitis. A few weeks later there was spastic paralysis, and the diagnosis was changed to Pott's disease. The patient remained paralyzed; about eighteen months later I saw her. The history seemed peculiar to me, and I had a roentgenogram made, which showed a small defect in the fourth thoracic vertebra. I thought this region should be explored, and Dr. Ryerson performed a laminectomy and observed a small epidural abscess. The patient made a complete recovery, which is strange after an illness of such long duration but shows that a few patients survive even if early operation is not performed. From experience in this case and in a few others I had the erroneous impression that epidural abscesses were commonly preceded by osteomyelitis, but I realize that this is not the case.

DR. LOYAL DAVIS: The epidural abscess in case 1 was easily located. It extended into the paravertebral muscles to the right of the spinal column; just as I was about to close the incision I noticed a drop of pus coming from the spinal needle wound in the dura. I opened the dura mater and drained a small amount of pus from the subdural space. As Dr. Gasul said, this boy had had multiple abscesses of the skin; about six months later there developed metastatic osteomyelitis in the radius, which was opened and drained. The boy is now in good condition.

I saw another case of acute epidural abscess in an older patient, which resulted from a small furuncular abscess on the knee. I observed another patient, who evidently had an epidural abscess which ruptured through the skin and drained itself. I saw the last-mentioned patient for the first time two years later, when he had a definite lesion of the spinal cord. At operation adhesive arachnoiditis was observed. This brings up the question whether Dr. Gasul's patient may not yet show similar signs of obstructive lesion.

DR. ERIC OLDBERG: Although Dr. Gasul has mentioned it in his report, I wish to emphasize the emergency character of acute epidural abscess. Preparations for operation should be undertaken as soon as the diagnosis is made. To delay even a few hours is to run a high risk of permanent damage to the cord. In the patient (case 2) of whom I had charge with Dr. Gasul, symptoms of involvement of the cord had been present for four days; although I performed an operation on the evening I saw her, she has a permanent total transverse lesion. Another patient

whom I saw with Dr. Hedblom was operated on five hours after the first appearance of symptoms (paresthesia in the legs) and yet nearly six months elapsed before the patient regained normal control of the lower extremities.

I presume the rapidity with which softening takes place is a feature more of inflammatory reaction than of unusual pressure. That has been my belief with regard to the explanation of the permanence of damage to the cord associated with malignant metastases to the spine. My experience has been that in these cases, even though decompression is done early, there is likely to be a delayed or incomplete recovery, in contrast to the results obtained in removing benign lesions, such as meningioma, which may have exerted great pressure over a long period.

DR. BENJAMIN BOSHES: In regard to the comment by Dr. Davis, I wish to describe a little further the case that was reported to this society two years ago—that of a woman in whom an epidural abscess developed from a furuncle on the knee. She was operated on by Dr. Davis and made a rapid and complete recovery. Pus was observed epidurally, subdurally and in the subarachnoid space. The interesting feature in the case is that a year later the patient complained of pain in the legs, in the distribution of segments from the fourth lumbar down, with corresponding motor changes. Examination disclosed complete block of the spinal fluid. Diathermy was applied to the back and physiotherapy to the paretic muscles. The symptoms gradually receded. The patient now does work in which she is required to be on her feet most of the day, and no signs of trouble are to be found at present.

DR. MEYER SOLOMON: Stanley described two cases of this sort (*Illinois M. J.* **68**:515-517 [Dec.] 1935) in one hospital at the same time. About a year and a half ago I was called to a Chicago hospital by a physician, who told me that operation for appendicitis had been performed on a girl about 16 years of age; there had then developed paralysis of both lower limbs. When I saw her she had flaccid paralysis, loss of both superficial and deep sensation, and intense pain radiating into the abdomen. The physician was sure she had not had appendicitis, for which the operation had been performed. Spinal puncture revealed a block. The next morning the patient was taken to another hospital under the care of a neurosurgeon, and an epidural abscess was observed.

DR. BENJAMIN M. GASUL: I wish to thank those who have taken part in the discussion and particularly Dr. Hassin for enlightenment on the pathologic features of the condition.

COMPARATIVE VALUE OF VARIOUS METHODS OF REDUCING INTRACRANIAL PRESSURE.

DR. JULES H. MASSERMAN (by invitation).

Slow drainage of small amounts (from 15 to 20 cc.) of spinal fluid is an effective and safe means of reducing intracranial hypertension, except in the comparatively rare instances in which there is danger of producing cerebellar herniation. In cases of comparatively high original tension, the drainage of small amounts of fluid is proportionately more effective.

Rapid drainage of large amounts of fluid (35 cc. or more) is contraindicated because of the danger of inducing cerebral congestion and edema.

Intravenous administration of hypertonic solutions of dextrose produces, after an initial rise, the desired fall in cerebrospinal fluid pressure. However, after from two to four hours this decompressive effect is succeeded by reactive intracranial hypertension, which may cause exacerbation of the original symptoms.

Hypertonic solutions of sucrose are cheaply and easily prepared; they are nontoxic when administered intravenously, and if given in sufficient amount and concentration (from 200 to 500 cc. of a 50 per cent solution) they produce a marked and sustained diminution in intracranial tension, which is not succeeded by a dangerous secondary rise. Hypertonic solutions of sucrose can be injected repeatedly and apparently offer one of the most satisfactory means to date for reducing intracranial hypertension.

DISCUSSION

DR. HANS H. REESE, Madison, Wis.: I am much interested in the work of Dr. Masserman. For dehydration I use a 50 per cent solution of sucrose only,

and in my experience the results have been much more gratifying than those with 50 per cent dextrose. I believe that hypertonic dextrose solution reduces effectively the cerebral fluid pressure, but I dislike the secondary rise following the initial reduction in pressure. I agree with Dr. Masserman's statement that dextrose diffuses readily into the cerebrospinal fluid and brain and that even when the concentration in the blood stream falls the brain will remain hypertonic and edematous. The conclusions of Gregersen and Wright that sucrose cannot pass the barrier between the blood and spinal fluid and that its administration does not result in hyperglycorrhachia or a secondary elevation in pressure have led me to use sucrose instead of dextrose.

Small amounts of cerebrospinal fluid withdrawn by spinal or cisternal puncture are often beneficial in cases of increased intracranial pressure, although present teaching condemns lumbar puncture in cases of increased intracranial pressure.

DR. BENJAMIN BOSHES: I wish to ask about the method of manometry used in the first part of the experiment, in which Dr. Masserman described a large drop in cerebrospinal pressure after small injections of the solution of sucrose. Was not that because he was using relative instead of absolute manometry? Kilgore, and others before him, demonstrated this in connection with the absolute and relative manometer.

DR. JULES H. MASSERMAN: All the manometric readings were corrected with those of a bubble manometer.

SYNDROME OF OCCLUSION OF THE ANTERIOR SPINAL ARTERY DUE TO ARTERIOSCLEROSIS. HOWARD ZEITLIN and BEN W. LICHTENSTEIN (by invitation).

This paper will appear in full, with discussion, in a later issue of the ARCHIVES.

PHILADELPHIA NEUROLOGICAL SOCIETY

Stated Meeting, Nov. 22, 1935

F. C. GRANT, M.D., *President, in the Chair*

LATE RECRUDESCENCE IN EPIDEMIC ENCEPHALITIS (ENCEPHALITIS LETHARGICA), WITH SUCCESSION OF NEW MANIFESTATIONS AT INTERVALS OF YEARS: THE PROBLEM OF PROGNOSIS. DR. ALFRED GORDON.

It is established that the virus of epidemic encephalitis may invade any area of the central nervous system but that it has a special affinity for the striatal region of the midbrain. The parkinsonian symptom group is the usual clinical expression of the disease. As to the so-called sequelae, the literature shows a multiplicity of phenomena in different spheres of human organization. The sensory system, the special sensorium, the motor system, the psychic functions and the affective state—all may show morbid alteration. There are cases in which one observes aggravation of preexisting symptoms, as well as the occurrence of new ones. They can signify only progressive and extensive development of the original lesion, due, in all probability, to the persistence of the encephalitic virus in the nerve tissue. The clinical history in many cases indicates that the virus may remain active in the nerve tissue for a considerable time and that it is capable of creating new anatomic lesions and of extending preexisting ones. Present therapeutic resources are too insignificant to effect neutralization of the virus and regression of the anatomic lesions and, consequently, modification in the course of the syndrome. The postencephalitic manifestations should be considered not merely as sequelae but as forms of a genuine chronic evolution in the presence of a virus which is still active.

The possibility of reawakening the old inflammatory process and the succession of pathologic manifestations in the same subject at intervals of years demonstrates that the sequelae are not of evolutional character but are late and definite phenomena, especially characteristic of epidemic encephalitis. This observation proves that it would be erroneous to assume a final position as to the course of epidemic encephalitis in a given case, even after the parkinsonian syndrome becomes definite. Such a contention is proved by the two cases to be described. Besides my main object in reporting these cases, namely, to emphasize the necessity of a reserved prognosis, I wish to call attention to new and unusual features which have not yet been recorded in the literature as late occurrences in association with epidemic encephalitis of long standing.

REPORT OF CASES

CASE 1.—M. P., a newspaper dealer aged 35, fifteen years prior to the time of examination had a condition characterized by acute onset, somnolence, fever and double vision. He was bedridden for four weeks. He then presented the attitude characteristic of the parkinsonian syndrome after an acute attack of epidemic encephalitis. The condition remained unaltered for six years, when there developed the oculogyric manifestations from which he still suffered when I saw him. He was unable to overcome this condition. Seven months prior to examination, that is, over fourteen years after the acute attack, there developed another disorder: At almost every meal, while masticating food, he experienced sudden rigidity and immobility of the tongue and was unable to roll the food from side to side. This sometimes lasted as long as from five to ten minutes. Three months before his examination he experienced sudden closure of the eyes, which, like the other symptoms, might appear without warning. Any effort on his part to open the eyes was useless. This manifestation lasted a shorter time than the upward movements of the eyes but, like the latter, incapacitated him and interrupted his work.

CASE 2.—S. S., a girl aged 20, had had a typical attack of epidemic encephalitis seven years prior to the time of examination. Shortly afterward she observed stiffness of the jaw and, later, impediment of speech. The condition progressed and up to the time of this report had remained stationary. The disorder in speech presented certain unusual features. Briefly, while the patient was speaking the tongue protruded between the teeth, rolled, curled and moved to the right side; at the same time two deep furrows appeared on the sides of the mouth. There was no evidence of aphasia, paraphasia or anarthria. Because of the dysfunction of the tongue, the food remained in the mouth a long time, and there was pronounced salivation. Simultaneously with the disorder in speech, myoclonic contractions of the muscles of the left hand appeared. Somewhat later, tremor was observed in the same hand. During four years the speech manifestation and the tremor of the left hand were the only postencephalitic sequelae. At the end of the fourth year the patient began to observe gradually developing weakness of the right upper extremity. One year before the time of examination, that is, six years after the acute attack, she noticed for the first time a tendency to turn her head to the left. This condition gradually increased in frequency and intensity so that at the time of writing typical spasmodic torticollis was present. The right leg, in addition to the exaggerated knee jerk, presented at the time of examination an extensor plantar reflex, a condition which was not present two years before.

In this case, as in case 1, there were several encephalitic sequelae, developing at long intervals and demonstrating the existence of latent or silent periods of years after the acute attack. Therefore, a final fixed stage in the disease under discussion cannot be admitted.

Comment.—The two cases are instructive from the standpoint of the prognosis of epidemic encephalitis, which is to be made guardedly even years after the onset, as recrudescence may occur at any time in the patient's life, with involvement of any part of the central nervous system. The so-called sequelae indicate the chronicity of the pathologic process and the persistence of the virus.

DISCUSSION

DR. D. J. MCCARTHY: I wish to ask Dr. Gordon what is his conception of the pathologic process in the general virus infection which he has described. I might say that it is not uncommon to have parkinsonism that is stationary; with what appears to be a cold or other infection there may be a flare-up of the process and recrudescence of symptoms. That form is, I think, different from this new process which Dr. Gordon has described. Is this latter form the same as the original process with which all physicians have had experience, or is it new?

DR. A. GORDON: Since in case 2 a gradual myoclonic condition developed in the right arm and later in the left and then the extensor plantar reflex appeared, the pathologic process was originally in the midbrain and did not start as a cerebral lesion. The hypertonic movements usually are considered to be due to pathologic involvement of the midbrain. The paretic symptoms are generally referred to lesions in the pyramidal tract. On each occasion something new appeared in the distribution of the postencephalitic condition.

In case 2, eight years after the acute phase hypertonic movements of the neck developed, which were probably related to the first attack of epidemic encephalitis.

I am inclined to believe that the virus was probably revived a first, a second and a third time, involving different brain tracts on each occasion. My main object in this presentation was to call attention to the guarded prognosis that should be made in cases of epidemic encephalitis, even when there is apparent recovery from the acute manifestations. The patient in case 1, like that in case 2, had parkinsonism for a long time, but later there developed one symptom and then another, showing that gradually, through a period of years, new symptoms may appear.

CASE OF TONIC TORTICOLLIS RELIEVED BY FEVER THERAPY. DR. BERNARD A. HIRSCHFIELD and DR. J. C. YASKIN.

This case is reported for several reasons: (1) the condition presented the picture of acquired tonic torticollis; (2) the symptoms and objective findings suggested the possibility of both an organic and a psychogenic etiology, and (3) the condition was completely relieved by fever therapy.

REPORT OF CASE

History.—R. F., aged 43, complained at the time of the first observation in May 1935 of stiffness of the neck, with a tendency to hold the chin to the right, and spells of faintness and confusion when an attempt to turn the head to the right was made. The family history was irrelevant. Aside from influenza in 1918, the past medical history was not important. The patient drank and smoked in moderation. He reached the second year of high school at 14, went to business college for another year and then began work in a pottery. Here he worked for twenty-seven years, becoming superintendent of production. When the depression came, he lost this job and with it quite a little money which he had accumulated. Since, he had had various positions and for the two years prior to examination had been supervisor of laborers for the state department of highways. He was married at the age of 22 to a Protestant girl, who adopted Catholicism for his sake. Almost from the beginning his marriage was unhappy from a sexual standpoint and for other reasons. Eleven years prior to the time of examination he met Helen, with whom he fell in love. He left his wife and went to live in a room, where Helen visited him. Helen was herself married and had two children. Though the husband knew that she was living with the patient, the arrangement seemed to be satisfactory. As a result of this association the patient had not practiced the Catholic religion for nine years. Six years before the time of examination, when his mother died, he was given to believe that her death was the result of grief over his unusual mode of living. For this reason he rejoined his wife and lived under the same roof with her for six months, but he then returned to his room and Helen.

In December 1934, while washing, the patient had a peculiar sensation in the legs and almost fell. He recovered from this spell promptly but noticed that he could no longer lie on his right side, although this was a lifetime habit. In February 1935 he had another attack, after which he began to hold his head with the chin directed to the right. The spells became more frequent, occurring every five to seven days. The attacks were described as a "feeling of weakness in the legs and momentary confusion." They were not accompanied by dizziness, double vision or loss of consciousness. In most instances the attack lasted only a few seconds, but on one occasion it continued, with intermissions, for about twenty minutes. When the patient assumed a reclining position or turned the head sharply to the left the spell could be made to disappear. He ate in a reclining position and walked and turned to the left rather than to the right, for fear he would have a spell. Observers noticed that he never fell during these attacks but sat down carefully, never changing color or losing consciousness.

Examination (June 26, 1935).—There were no significant physical abnormalities. The patient held his head in a fixed position, with the chin turned to the right and slightly downward. In this position there was spasm of the left sternocleidomastoid muscle and of the deep muscles of the neck on the right. The spasm was of tonic nature. No clonic movements were observed. There was no tenderness, and at no time was there any pain in the neck. In walking the patient held his neck rigid in the position described. He was fearful that he would have an attack if he should attempt to move his head. The fundi showed moderate angiosclerosis. The visual fields were normal. There was loss of hearing of 18 per cent on the right and of 12 per cent on the left; this was ascribed to chronic catarrhal otitis media. The caloric and Bárány turning tests revealed no evidence of intracranial lesion. All other cranial nerves, as well as the eighth, were normal. Detailed examination of the trunk and extremities revealed no abnormality in the motor, trophic, tonic, sensory, reflex or synergic sphere.

An attack was induced by turning the chin sharply to the right. All that could be observed was considerable anxiety, flushing of the face and hypotonus of the four limbs. The Babinski sign was not present during the so-called attack.

The patient showed no evidence of a psychosis. His intellectual grasp seemed to be normal. He realized that he had deviated from his faith but felt that he was doing no great injustice to either God or man. He had no fears except that he might lose Helen by reason of his illness, financial reverses and increase in age. He showed no evidence of overt anxiety or depression. He identified Helen with his mother and stated that she resembled the latter physically and in other ways and that she was the only woman he had ever loved.

Laboratory Findings.—Roentgen examination of the skull and of the cervical and dorsal portions of the spine revealed no abnormality. Lumbar puncture revealed an initial pressure of 10 mm. of mercury, with free rise and fall on coughing and straining and on compression of the jugular vein. The cerebrospinal fluid was clear and contained 2 cells, and there was no increase in globulin. The colloidal gold curve was flat, and the Wassermann reactions of the blood and spinal fluid were negative. Urinalysis, a complete blood count and studies of the blood chemistry (dextrose and urea nitrogen) gave normal results.

Course of Illness and Treatment.—A diagnosis of tonic torticollis due to a condition of the central nervous system was made. Although there were abundant psychogenic factors and no definite evidence of organic disease of the brain, it was thought that from the standpoint of therapy the condition should be regarded as encephalitis involving the basal ganglia. On this basis fever therapy was commenced. Intravenous administration of typhoid-paratyphoid vaccine combined with the use of the thermic pack was the method employed. Ten courses were administered, one every other day, the temperature reaching to between 104 and 105 F., where it was maintained for from four to five hours. Improvement in the spasticity of the muscles was noted after the second course and was continued with each course. At the time of discharge on Aug. 1, 1935, there was no torticollis; the

cervical movements were free, and the patient no longer experienced attacks. After regaining the weight lost as a result of the fever therapy, he returned to full duty. Several examinations revealed no evidence of recurrence.

Comment.—Acquired tonic torticollis is rare except as a secondary symptom in association with rheumatic myositis, organic disease of the cervical vertebrae, the Klippel-Feil syndrome and, in a mild form, neoplasm of the posterior cranial fossa and upper part of the cervical region. These conditions were not present in this case, and the cause was regarded as of central origin. Except when the disturbance is accompanied by other evidences of organic disease of the brain, as in diffuse encephalitis or dystonia musculorum, the etiologic diagnosis of acquired torticollis of central origin is always difficult. In the case reported the character of the spells and the rather complicated situational background suggested a psychogenic etiology. The absence of anxiety would not disprove such an assumption, as torticollis may be regarded as a conversion symptom (Yaskin, J. C.: The Treatment of Spasmodic Torticollis with Special Reference to Psychotherapy, with Report of a Case, *J. Nerv. & Ment. Dis.* **81**:299 [March] 1935). Because of the inherent difficulties of the protracted and expensive psychotherapy required in a case of this sort and because of the doubt regarding a possible organic etiology, fever therapy was attempted. Since there is still doubt about the etiology, it is impossible to state why the condition was relieved. It is not at all impossible that the fever treatment acted as a method of suggestion. In view of our experience in this case fever therapy deserves a trial when the etiology is in doubt and the duration of the disease is relatively brief.

DISCUSSION

DR. D. J. MCCARTHY: My experience has been unfortunate from the point of view of surgical treatment. I cannot say how the majority of patients react to psychologic treatment. Persons with this condition were seen frequently during the World War. It seemed that in many instances the disturbance was a habit spasm; for instance, a soldier lying in a bed next to that of a man who had been shot and was a horrible sight always kept his head averted in order not to see the other patient. Afterward, he seemed unable to keep his head from turning in the same direction, as though he were still trying to shut out the picture. I think that in most cases torticollis would disappear on interpretative suggestion and therapy. Surgical therapy has not been altogether satisfactory; often after surgical therapy I have had to continue with psychotherapy to get results.

DR. ALFRED GORDON: The case reported is dramatic, and, as Dr. Grant stated, treatment seems to be a question of psychotherapeutic influence. This man had suffered from torticollis for about one year with no relief, and then, when unusual treatment was instituted, he was relieved. I know of a woman who for a long time had paresis of the left arm. She was advised that she would regain its use by having injections of cold water. This treatment was given, and she recovered. In another case an intelligent professor who had had spasms of difficulty in swallowing without relief recovered with the use of a small quantity of an anesthetic which he was told would help him. The results in all these instances prove that psychotherapy is effective in some cases. It is of interest that all kinds of psychotherapeutic measures, slight or severe, may bring positive results in cases of functional disturbance.

DR. B. J. ALPERS: The problem of the etiology of torticollis is confused, and I have been greatly interested, in listening to this discussion, to find that many physicians regard torticollis as of psychogenic origin. This may be true in large measure, but not in all instances. However, the case for the organic etiology of torticollis does not rest on a very firm foundation. Investigators who regard it as due to a lesion of the striatum have never been able to prove that this condition develops later into typical dystonia lenticularis, of which the torticollis is said to be a fraction. The pathologic basis for the assertion rests on a case reported by Foerster, in which pathologic changes were observed in the striatum. While I should like to regard torticollis as an organic syndrome, I cannot accept the rather

flimsy evidence so far presented. Probably in most cases the disturbance is psychogenic, but I think that in some the disease may eventually prove to be organic. Certainly, in most instances the condition is refractory to treatment.

DR. W. L. LONG: Has there been any change in this patient's conditions at home? Has the family accepted his mode of living, so that he does not have the acute conflicts that he had formerly?

DR. F. C. GRANT: I think Dr. Yaskin will remember a man we saw in Dr. Weisenburg's service who had spasmodic torticollis. He had been without a job and was not happy. In this case we cut the spinal accessory nerve extradurally, without much effect. The patient secured a job in which he had to lift 140 pounds (63.5 Kg.) of coal onto his right shoulder. We saw him eleven months later. He had gained 30 pounds (13.6 Kg.) in weight in the meantime. The torticollis was relieved. I think that the hard work and the improvement in mental attitude may have cured him. I have seen a good deal of surgical intervention in the treatment of spasmodic torticollis, and I must say that the results scarcely justify the severity of the surgical means required to relieve this condition. I wish to ask Dr. Yaskin whether he thinks that this patient was improved because of the fever therapy or because of the psychotherapy incidental to the fever therapy? I am not at all convinced of the advisability of surgical treatment for torticollis. I think it is fortunate that this man did not fall into surgical hands. I should like to know whether any one has had experience with torticollis and what that experience has been. Usually, surgeons are asked to see these patients with the idea of radical therapy in mind.

DR. J. C. YASKIN: In reply to Dr. Long: The patient had definite conflicts for many years, and the acuteness of these conflicts was reached about six years ago, when his mother died and he felt responsible for her death. I was unable to ascertain anything that would cause aggravation of his condition in the past year. I do not know whether or not the condition was of organic origin and whether the fever treatment acted on a possible encephalitic lesion or by suggestion. The general medical literature of recent years conveys the impression that torticollis in every case is a neurosurgical problem. The psychoanalytic literature regards the origin in every case as entirely psychogenic. O. Foerster (*Verhandl. d. deutsch. orthop. Gesellsch.* **23**:144, 1928) expressed the opinion that in every case torticollis is of organic origin and that the basal ganglia are always involved, so that even psychogenic factors produce torticollis by acting on congenitally predisposed basal ganglia. My own position in regard to this question is the same as that in respect to the cause of chorea. In the majority of instances chorea is of infectious origin, and yet every physician has seen cases in which no definite infection could be proved and in which the disease was precipitated by emotional strain. I can never be sure as to the origin of torticollis when it occurs as an isolated symptom. In the presence of other evidences of encephalitis the diagnosis is easy. When it is a part of a psychoneurosis the etiologic diagnosis is likewise not difficult. The important feature in this case is that at least temporary relief was procured by means of fever therapy, a procedure which is less time consuming and less expensive than psychotherapy and less painful and less dangerous than neurosurgical intervention.

PUPILLARY REACTIONS IN EXPERIMENTAL LESIONS OF THE MIDBRAIN. DR. E. SPIEGEL and DR. N. SCALA.

Combined lesions of the posterior commissure and of the central pupillodilator tracts were produced in cats, and the effect of such lesions on the pupillary light reflex, the response to painful and emotional stimuli and the reaction of the pupil to instillation of atropine were studied. It was found that unilateral severance of the posterior commissure induces slight homolateral mydriasis and diminution, but not loss, of the light reflex. If this lesion is combined with one of the central portion of the pupillodilator pathways, slight miosis of the homolateral pupil results; the dilator response of the corresponding pupil to painful or emotional

stimuli is diminished but not abolished, and after instillation of atropine in both eyes the miotic pupil dilates somewhat more slowly than the opposite pupil, but finally to nearly the same extent. Such combined lesions do not produce the picture of the Argyll Robertson pupil in cats as far as the reactions mentioned are concerned. The assumption of a lesion at the synapse between the afferent and the efferent part of the pupillary light reflex arc offers the best explanation for all the symptoms of the Argyll Robertson pupil.

DISCUSSION

DR. F. H. LEWY: Dr. Spiegel stressed the fact that lesions of the descending tract from the hypothalamus do not concern pupillary reactions. This is corroborated by my experience that destruction of the pupillary center in the corpus Luysi produced a temporary pupillary disturbance, which completely disappeared in a week or two.

EMOTIONS AS THE CAUSE OF RAPID AND SUDDEN DEATH. DR. N. S. YAWGER.

Years ago, a medical periodical in India published an article entitled "Killed by the Imagination." In substance it stated: A celebrated physician, author of a work on the effects of the imagination, was permitted to try an astonishing experiment on a criminal who had been condemned to death. The prisoner, an assassin of distinguished rank, was advised that, in order that his family might be spared the further disgrace of a public hanging, permission had been obtained to bleed him to death within the prison walls. After being told "Your dissolution will be gradual and free from pain," he willingly acquiesced to the plan. Full preparations having been made, he was blindfolded, led to a room and strapped onto a table near each corner of which was a vessel containing water, so contrived that it could drip gently into basins. The skin overlying the blood vessels of the four extremities was then scratched, and the contents of the vessels were released. Hearing the flow of water, the prisoner believed that his blood was escaping; by degrees he became weaker and weaker, which, seemingly, was confirmed by the conversation of the physicians carried on in lower and lower tones. Finally, the silence was absolute except for the sound of the dripping water, and that too died out gradually. "Although possessed of a strong constitution [the prisoner] fainted and died, without the loss of a drop of blood."

While the emotions have an evident relationship to the development of certain physical diseases, psychoneurosis, some forms of psychosis and crime, as well as a significance in every day life, they receive rather scant consideration, either through lack of knowledge or through neglect. One may find present day neurologists speaking of the mental and emotional conditions of the patient, unmindful of the fact that the latter are an integral part of the former, since the intellectual and emotional processes together constitute the mental state. Whether man is dominated more by his reasoning or by his feelings is a question. Older authors showed greater cognizance of emotional values, and there come to mind the names of Rush, Sweetser, Carpenter, Tuke and Brown-Séquard.

Tuke referred to the case of the criminal just cited when he wrote: "But it is impossible to say how much fear had to do with it; probably a great deal, as in the case of the man reprieved, after his head had been laid upon the block, and the fatal ax was about to fall. The reprieve came too late. The anticipation had arrested the action of the heart. Death predictions belong to a class in which fear may enter largely, and yet in some instances it seems to have been simply a strongly impressed idea unattended by fear. How far, however, death happens through arrest of the heart's action, one cannot say but it seems by far the most likely cause."

Dunbar, in discussing "psychogenic cardiac death," referred to death among primitive tribes, in persons who believe they have overstepped a taboo, and added: "Many cases have been reported where patients in good health died on the operating table before the anesthetic was administered."

Carpenter, in an article on expectant attention, stated: "This persistent direction of the attention has a much greater potency when combined with the *expectation of a* particular result: and thus it happens that the spells of pretenders to occult powers, in all ages and nations, often produce the predicted maladies in the subjects who are credulous enough to believe in their efficacy. Such was formerly the case amongst the Negroes of the British West Indies, to such a degree that it was necessary to repress what was known as 'Obeah practices' by penal legislation; a slow pining-away, ending in death, being the not uncommon result of the fixed belief on the part of the victim, that 'Obi' had been put upon him by some old man or woman reputed to possess the injurious power. So great, indeed, was their dread of these spells, that the mere threat of one party to 'put Obi' upon the other, was often sufficient to terrify the latter into submission. And there is adequate ground for the assertion, that even amongst the better instructed classes of our own country, a fixed belief that a mortal disease had seized upon the frame, or that a particular operation or system of treatment would prove unsuccessful, had been in most instances the real cause of a fatal result."

A Negro people on the west coast of Africa were thus described by Schofield: "I have been told by a naval surgeon from an African squadron that Kroomen, if badly treated or angry, will threaten to die; and will go away and finally expire in thirty hours without any injury or disease." Among other African tribes similar effects are described. Weeks stated: "The witch doctor is the arbiter of life or death, for not only is the victim he selects led away to drink the ordeal, but so implicitly do the people believe in him that, when he says his patient will die, this invariably happens, as his friends at once begin to prepare for the funeral, and instead of feeding the patient, they dig his grave and send to call his relatives to the obsequies. The medicine-man has said he will die, so what is the use wasting time and food on him."

Owen stated: "It really is not necessary for a voodoo to have great knowledge of poisons, for such is the power of suggestion upon the ignorant and superstitious that if a Negro imagines that he had been 'hoodooed,' 'witched' or 'conjured,' he pines away and dies unless someone is found whom he considers a voodoo of greater powers to minister to his diseased mind and root out the death-compelling terrors by the tricks and baubles of his nefarious profession. Few white people realize the menace of voodoo due to its absolute power of a certain class of mind."

Reid wrote: "In Lasinsky's voyage around the world, there is an account of a religious sect in the Sandwich Islands, who abrogate to themselves the power of praying people to death. Whoever incurs their displeasure receives a notice that the homicidal litany is about to begin; and such is the effect of the imagination that the very notice is frequently sufficient, with these people, to produce the effect." Strecker and Appel contributed the following: "It has been authoritatively related that on one of the South Sea Islands where voodooism is practiced, strong, healthy young natives died a few weeks after they had been told that a gum-tree image of themselves had been fashioned by a voodoo priest, thrust through with a sharpened twig and melted in a flame. If this is true, it is an example of emotional death."

Among the western Indians of this country, when a medicine-man utters a withering curse on his antagonist, the latter knows all hope is lost. He sometimes drops dead on the spot.

In secret societies rare instances are encountered in which it appears that death came to candidates through the application of nonlethal shock. An iron molder and the president of a local chauffeurs' union were being initiated into the Order of the Moose. After they had been blindfolded and their chests made bare, it was dreadfully announced that they were to be branded. A metal emblem to which a wire was attached was applied to each man's chest and on receiving the customary shock both collapsed with fright and the lodge physician was unable to revive them.

Sweetser, writing on "Pleasurable Passions," gave as instances in which a person died of joy the deaths of Diagoras, Dionysius and Pope Leo the Tenth and, possibly, that of Sophocles. Rush cited many instances of death from joy

and among others mentioned that of the son of Leibnitz, who, on opening an old chest and unexpectedly finding in it a large quantity of gold, suddenly expired. Sir Thomas Urquhart is said to have died of laughter on learning that Charles the Second had regained the throne.

Under the caption "Death from Mental Excitement," an instance was recorded in which the reactions from the mingled emotions of anxiety and joy were followed by sudden death. A woman aged 43 heard the alarming report that many persons had been injured in an accident to a train on which her daughter was a passenger. The mother, arriving at the station in time to see her daughter emerge unharmed, threw her arms about her, fell into a fit and expired a few hours later.

Buddle, speaking of treatment for snake bite in regions where poisonous reptiles abound, stated: "In this connection, however, it cannot be too strongly insisted upon that it is of paramount importance to be able to determine whether the bite is due to a harmless or a poisonous snake, since it is well known that many persons have died from fright after having been bitten by a harmless or a non-lethal snake."

In referring to persons who die of grief, Carpenter cited a case, though not one of his own, in which two sisters were deeply attached. One acquired tuberculosis and died; she had been tenderly cared for by the other, who, seemingly, had suppressed her sorrow. About a fortnight later the surviving sister was found dead in bed. There had been no symptoms during life, and at autopsy there was no evidence of disease. Death was attributed to the depressing influence of pent-up grief. Carpenter, quoting Carter, an authority on hysteria, described the case of a woman who saw her son accidentally lose three fingers; she was so overcome that she could not render assistance. A surgeon, who had responded promptly, turned to find the mother moaning and complaining of pain in her hand. Examination disclosed that the three corresponding fingers of her own hand, which had previously been normal, were swollen and inflamed. In twenty-four hours pus was evacuated, and the wound ultimately healed.

In writing of animal life, Penrose stated: "It is not merely speculation to discuss the physical effects of the emotions on the animal body. It has been shown that fear, anger and grief bring about distinct measurable physical changes." Dr. Corson-White observed that the red corpuscles were increased by over 2,000,000 per cubic centimeter in a cat frightened by the barking of a dog. The amount of sugar was also increased. Such observations are suggestive in a consideration of the changes that may occur in a captive animal subjected to acute and chronic fear. Nostalgia may cause death. Negroes and the American Indians are more afflicted than white persons in this way. On the induction of fear in a subject under hypnosis, Pedersen reported that definite changes were observed in the pressure, chemical and cellular composition of the blood and in the pulse rate.

In speaking of the death of oxen through grief, an author stated: "They are those old workers who, through long habit have grown to be *brothers,* as they are called in my country, and who, when one loses the other, refuses to work with a new comrade, and pines away with grief. People who are unfamiliar with the country call the love of the ox for his yoke-fellow a fable. Let him come and stand in the corner with one of these poor beasts, thin and wasted, restlessly lashing his thin flanks with his tail, violently breathing with mingled terror and disdain on the food offered him, his eyes always turned toward the door, scratching with his hoof the empty space at his side, sniffing the yoke and chains which his fellow used to wear, and incessantly calling him with melancholy lowings."

Metchnikoff stated: "Fear, which is occasionally able to excite contraction of the involuntary muscles, also stimulates other muscles against the will."

In writing of the characteristic marks of fear, Ribot spoke appreciatively of the work of Lange, who stated: "As regards the vasomotor apparatus: a spasmodic contraction of the vessels, shivering, violent spasm of the heart; and if the impression is of excessive violence, paralysis which may end in death . . ." Emerson, in a discussion of efforts to include the emotional factor as a cause of disease, stated that physicians "have done their best to enlist the aid of the emotional life of their patients in their therapy, and their results, when successful, have been

ascribed to 'power of the personality,' 'suggestion,' 'psychotherapy,' etc., terms which until recently implied criticism that a 'regular' physician should stoop to such practices, but the trend in medicine is to subject the emotional factor to psychological research which often proves fruitful. It is now realized that under certain conditions a strong emotion can inflict a physical trauma (injury) just as directly as can a knife."

Organic lesions result from such functional states as hypnosis and hysteria; under the powerful emotional pressure of horror, the hair is frequently reported to have whitened rapidly, as in the case of Marie Antoinette, guillotined in 1793, and in that of Henry M. Stanley, who himself said that his hair turned white in that distracting historic night when, without their existence having been previously known, pygmies suddenly attacked him in northeastern Africa.

Necropsy does not always give convincing evidence of the cause of death. Just what the psychopathologic or the anatomicopathologic condition may be in these cases is not clear. Perhaps death may be due at times to spasm of the heart produced by disturbance of the autonomic nervous system or, as Brown-Séquard attributed it, to paralysis of the medulla.

From the primitive and superstitious peoples of Africa, the Sandwich Islands, the West Indies, North America and elsewhere have come many reports of rapid or sudden death through fear or horror; in some instances there may also have been what Carpenter termed expectant attention.

In consideration of the many strange instances of death, can the subject be dismissed by attributing the event always to error, deception, collusion or poisoning? I do not think so. Doubtless, such devastating reactions are far less likely to occur among enlightened people. Nevertheless, enough cases are reported from trustworthy sources to give credence to the occasional occurrence among civilized peoples of death from rapid or sudden emotional reactions.

DISCUSSION

DR. D. J. MCCARTHY: I must say that in forty years of extensive experience I have never seen a case of death due to sudden emotion, though that does not mean that its occurrence is not possible.

DR. M. A. BURNS: I have been interested for a long time in the emotions of persons preceding death and, because of this, I attended an electrocution at the Pennsylvania State Penitentiary at Rockville, Pa. I was to witness two electrocutions the same morning, and my idea was not only to see the electrocutions but to talk with the prisoners before they went to the chair. This privilege was denied me by the warden. (I understand no one can see the convict for twelve hours before the electrocution except the spiritual advisers and the prison physician.)

One of the convicts was a Negro. To my surprise, he walked to the chair unassisted, sat down and had the electrodes attached and the current turned on, without any display of emotion. The second prisoner was a white man in the early fifties; he appeared so suddenly that I believe my emotions were more upset than his. He, too, walked unassisted to the chair, made no parting remarks and did not give vent to any emotional outburst. The electrodes were applied and the current was turned on without any display of feeling on his part. I think I suffered more—waiting for an emotional outburst that might have occurred—than did the condemned men. If emotion may be the cause of rapid and sudden death, the knowledge that he is condemned to die by violent means should be sufficient to cause enough shock to the emotions of the ordinary person to result in death, but in the instances which I have cited it seemed to have no effect. However, one must remember that the prisoners may have been hardened criminals whose instincts and emotions had become blunted.

DR. M. K. MEYERS: While perhaps such conditions do not occur in the more civilized peoples, I am sure that what Dr. Yawger said about the primitive and the somewhat advanced tribes is true. A year or two ago I heard a lecture by a man—half European and half Maori—who had lived in Polynesia and had done anthropologic field-work there. He stated that the influence of sorcery in that part

of the world is marked. If my memory serves me correctly, he, although trained in New Zealand and an anthropologist of note, admitted that he was somewhat afraid of spells which are cast among the natives of Polynesia. On one occasion, when he was visiting a foreign tribe, a sorcerer accosted him and threatened that charms might be used on him. The anthropologist told the sorcerer that, owing to the possession of certain tribal prerogatives, he, the anthropologist, was immune to the effects of the charms and knew that if charms were used on an immune person they would make the sorcerer rue anything he might attempt with them. Thereon the sorcerer became very sick and remained so for a time. There is no doubt that effects from known charm casting occur among these people, and it is probable, too, that such tribes ascribe much illness in general to the results of sorcery supposed to be carried out in secret.

I wonder if one cannot correlate the material in this paper with that of an article recently read before the Philadelphia Psychiatric Society by Dr. MacMillan, in which the deaths of certain patients with schizophrenia were reported, without postmortem observations which would account for them.

DR. J. W. MCCONNELL: I have in mind a case of which I had knowledge many years ago, that of a young man who was training to be a champion boxer. He was a magnificent specimen of manhood and was not lacking in courage. Two days before his expected match he had a slight hemorrhage from the lungs, and, as there had been cases of tuberculosis in his family, he sent for a physician, who happened to be I.

There were râles in the chest, but I could find nothing marked. I told him to stay in bed and keep quiet. As I was leaving the house the mother told me that the parish priest was coming and suggested that, as the young man had not been attending to his church duties for some time, it would be well for the priest to see him. Fearing that the patient might be frightened by the advent of the priest or his attempt to perform in a religious way, I cautioned the mother, but, nevertheless, the priest saw the boy and ill-advisedly, in my opinion, administered the last rites. This was at 3 p. m. The young man was terribly alarmed, and by 6 p. m. he was dead. The cause of death I do not know. As I had seen him about 10 a. m. the case was one in which a coroner's examination was required. The coroner pronounced his death due to the hemorrhage, but as this involved only a small amount of bleeding, I have always thought that, as the boy was afraid to die, aggravated fear when he was shrived so unexpectedly caused his death.

DR. N. S. YAWGER: I am glad to have had the opportunity of listening to this discussion. Rarely, there has been observed a patient with acute hypermania, formerly known as Bell's fulminating mania, who has died in a few days. It appears that no definite physical basis has been observed for this extremely devastating emotional disorder.

Regular Meeting, Dec. 28, 1935

FRANCIS C. GRANT, M.D., *President, in the Chair*

AN INTERESTING CASE FOR DIAGNOSIS. DR. MICHAEL SCOTT.

A boy aged 12 years was referred by Dr. V. K. Hart, of Charlotte, N. C., to Dr. Temple Fay on Dec. 5, 1935. He had been well until 6½ years of age, when his right eye began gradually to turn in and the right side of the tongue looked different. About one-half year later he began to have severe generalized throbbing headaches, not associated with any other complaints. These occurred every few months and gradually disappeared by 8 years of age, at which time he noticed impairment of hearing in the right ear and paralysis of the right side of the face. The paralysis of the face, which was intermittent at first, gradually became permanent; vision gradually failed in the right eye, and hearing became

worse. There was a short period, two years ago, when the patient had difficulty in speaking above a whisper, but this rapidly disappeared. There has been no difficulty in swallowing or breathing. The patient thought that he could taste better on the left side of the mouth. He complained of no other sensory or motor difficulties. The past medical history was normal except for infection with hookworm. The family history was of no importance.

Examination.—The patient was intelligent and cooperative. There was slight emaciation, and the head was rather large. There was definite tenderness on percussion in the right temporal region, with a cracked pot sound. There was some diminution in the sense of smell bilaterally but it was difficult to evaluate this since the patient had bilateral rhinitis. There was internal squint of the right eye, with definite paralysis of the right rectus muscle. The pupils were equal and dilated and reacted to light and in accommodation. The right optic disk showed atrophy, and the left disk, slight nasal blurring. The visual fields were normal in the left eye; the right eye showed marked impairment of vision. The corneal reflex was decreased in the right eye. The field of the trigeminal nerve in the face was not impaired. There was marked typical facial nerve paralysis on the right, including the forehead. In the Rinne test hearing was lateralized to the left. There was slight gross perception of hearing on the right; bone conduction was present but brief; air conduction was not present. The right side of the soft palate was paralyzed; the pharyngeal reflex was present bilaterally, but was more marked on the left. There were paralysis, atrophy and fibrillation of the right half of the tongue, with protrusion to the right. No definite impairment of swallowing, talking or taste was present. There was definite weakness of the right trapezius muscle, the deltoid and pectoralis muscles on the left being used on abduction of the right arm and in raising the shoulder. The deep tendon reflexes were present and equal in both the upper and the lower extremity, being more exaggerated in the lower. The Hoffmann and Babinski signs were absent. Sensation, coordination, stereognosis and muscle power were not impaired.

Ocular Examination.—Dr. W. I. Lillie and Dr. G. G. Gibson reported partial corneal anesthesia of the right eye and paralysis of the orbicularis oculi and the lateral rectus muscle on the right. Examination of the visual fields revealed concentric contraction in the right eye, with absolute central scotoma. The right fundus revealed pallor of the disk, with beginning primary atrophy of the optic nerve. The left fundus was normal.

Examination of the Ear.—Dr. J. S. Ersner reported definite nerve deafness on the right. The audiometer reading showed loss of hearing of 56.9 per cent in the right ear and of 15 per cent in the left.

Examination of the Nasopharynx.—Dr. R. F. Ridpath reported no change in the contour of the posterior wall.

Laryngoscopic Examination.—Dr. Chevalier Jackson reported complete loss of motility of the right vocal cord, the larynx otherwise being normal.

Laboratory Findings.—The results of the Wassermann and Mantoux tests and of urinalysis were normal. A complete blood count showed a marked decrease in hemoglobin, with a normal red cell count. The white cell count was within normal limits, but the number of eosinophils ranged from 10 to 20 per cent.

Daily examinations of the stools failed to reveal ova or parasites.

Summary.—In this case was shown progressive and gradual involvement of the second, sixth, seventh, eighth, ninth, tenth, eleventh and twelfth cranial nerves on the right side of at least five and one-half years' duration, with no symptoms at present of marked increase in intracranial pressure or of involvement of the pyramidal or sensory tracts except possibly slight involvement of the trigeminal nerve on the right.

DISCUSSION

DR. HELENA RIGGS: We recently performed an autopsy in another case in which the condition was similar. There were erosion of the bone and infiltration

of the dura, brain and tissues of the neck. The bone was undergoing absorption, however, rather than hyperplasia.

DR. TEMPLE FAY: I should like to have expressions of opinion as to what this condition may be.

DR. L. R. CHAMBERLAIN: The roentgenograms revealed a large shadow at the base of the skull on the right side. Its nature was not determined, but the possibility of a chordoma was considered.

NONTRAUMATIC SUBAPONEUROTIC CEPHALHEMATOMA. DR. MICHAEL SCOTT.

A girl, aged 14 years, was admitted to the neurosurgical service of Dr. Temple Fay on Nov. 20, 1935, with the chief complaint of painless, progressive swelling of the top of the head for about one week. Two weeks before her admission to the hospital, about Nov. 7, 1935, she fell down a flight of steps; she insisted, however, that she did not strike her head. One week later it was noticed that the left eye was puffed, and on the next day the right eye also became edematous. In two or three days the swelling receded in both eyes. A few days later the mother noticed that the child's head was getting larger; the persistence of this painless enlargement resulted in admission to the hospital about one week after the swelling of the head was noticed.

The past history was essentially unimportant except that the child had complained that her glasses were too tight around the ears and nose about two or three months ago. She had always been healthy. Her diet was fairly well balanced except that butter and orange juice were rarely served.

The family history was essentially without significance.

Physical Examination.—The patient was a comfortable, emaciated, dark-skinned, mentally retarded child, with a head of triangular shape. There was bulging over each temporal region and over the frontal bone. Palpation revealed a fluctuating mass which responded to gravitational positions and apparently surrounded the entire vertex. Through this fluctuating mass, especially over the frontal bone, small, painless, irregular or round, marble-like exostoses and ridges could be felt. A definite linear ridge could be felt on each side along the origin of the temporal muscle. There was no pulsation or evidence of inflammation. The teeth appeared to be well calcified, and there was no evidence of marked nutritional disturbance except the emaciation. The neurologic and physical examinations gave essentially normal results.

Laboratory Reports.—The urine was normal. The hemoglobin content was 11.5 Gm. per cubic millimeter. The red cell count 5,000,000, the color index 0.71 and the white cell count about 12,000, with 50 per cent neutrophils, 45 per cent lymphocytes, 3 per cent monocytes and 2 per cent eosinophils. The platelet count, coagulation and bleeding times and the results of the fragility test were within normal limits.

The Wassermann and Kahn reactions of the blood were negative in the patient as well as in the mother and father. The Mantoux test gave a negative reaction. The blood sugar, serum calcium and serum phosphorus contents were within normal limits.

Further Examination.—The patient was seen in consultation by Dr. W. W. Babcock, who stated that he was unable to advance any reason for the swelling of the scalp apart from overlooked trauma. Blood dyscrasia was ruled out. The patient was seen in medical consultation by Dr. John Lansbury, who stated that no general medical condition was found to account for the swelling of the scalp. He thought that subclinical scurvy should be ruled out.

Flat plates taken of the skull revealed essentially normal structure.

Five days after admission to the hospital aspiration of the scalp revealed 160 cc. of dark brown bloody fluid, which separated into a cellular and a serum layer. Immediately after the aspiration 140 cc. of air was injected in an effort to delineate any irregularities of the external portion of the skull. Fluoroscopic

and roentgenographic studies again showed essentially normal structure except that a fluid level was revealed over the temporal regions on one side.

Subsequent examination of the aspirated fluid by Dr. F. W. Konzelmann and Dr. Ernest Spiegel revealed chiefly red cells, with many clumps of macrophages, richly laden with iron pigment. No neoplastic cells were present.

Roentgenographic examination of the long bones and sternoclavicular joints showed nothing abnormal. Two weeks after admission an encephalogram was made, which revealed normal structure.

After the aspiration the swelling did not recur, and the patient was discharged three weeks after admission.

Summary.—Because this child persistently denied striking her head and because she complained of tightness of the glasses about her nose and ears two or three months before the onset of the present condition, it was concluded that one was dealing with a painless, progressive subaponeurotic hematoma of nontraumatic origin, of at least from two to three months' duration and of unconfirmed etiology.

DISCUSSION

DR. TEMPLE FAY: This is the first case in which I have seen anything of this sort. My colleagues and I examined the patient carefully and found a large, bulging, tense mass, which extended over the top of the head. We made an encephalogram, but nothing could be proved neurologically.

TENTORIAL DECOMPRESSION AND HIGH VOLTAGE RADIATION IN THE TREATMENT FOR MEDULLOBLASTOMA. DR. TEMPLE FAY.

The problem of cerebellar medulloblastoma in children is a distressing one to the neurologist and neurosurgeon alike. The period of survival without treatment averages less than one year. The majority of patients treated by surgical means alone (exploration, extirpation and suboccipital decompression) have died within two years, and those who have survived for a period of three years after any type of treatment are few. The 3 or 4 instances of survival for six years are outstanding exceptions and serve only to emphasize the rule.

Fortunately, tumors of this type are relatively uncommon. Cushing reported 81 cases in his series. Analysis of this group indicates that patients who received adequate high voltage radiation therapy survived for a definitely longer period than those treated by surgical means alone. Dr. M. C. Sosman was so impressed by the results of high voltage irradiation that he advocated and undertook this type of irradiation without operative intervention; he believes that when a cerebellar tumor of this type is suspected a therapeutic test with high voltage radiation should be given before surgical intervention is attempted, as symptoms rapidly disappear in cases of medulloblastoma, whereas lesions of other types do not respond. Surgical treatment for conditions of the latter type, with its attendant risk, may then be resorted to.

It may be of interest to recall that Spiller in 1927 advocated high voltage roentgen therapy for a child aged 2, with advanced symptoms of cerebellar tumor and pressure. No operative measures were resorted to, and the child rapidly became free from symptoms and remained so for two years; she returned then for operation, after which she died. At that time Dr. Pendergrass administered cross-fire doses of high voltage radiation, as the present Coutard method of fractional doses was not known. Dr. Sosman has recently emphasized the need of irradiating ventricular areas as well as the spinal axis.

In view of the improvements and advance in methods of high voltage irradiation and the increasingly good results obtained with these measures, I wish to present the observations which my colleagues and I made in a series of 8 cases over a period of five years, during which Dr. Chamberlain delivered to the tumor area a total of from 3,000 to 4,000 roentgen units in a series of treatments with fractional Coutard doses at intervals of from three to six months.

Of the first 4 patients in whom the usual suboccipital exploration and decompression were followed by high voltage irradiation, 1 has survived the three year period. In the others the extension of the tumor eventually produced insurmountable problems of increased intracranial pressure due to strangulation of the brain stem by the incisura, as a result of which the patient died. It seemed evident that if unrestricted space could be given the cerebral structures in the region of the incisura the roentgenologist might have additional time to attack the lesion and intracranial pressure might be controlled for a longer period.

In the second series of 4 cases it was decided to expose the cerebellar hemispheres in the usual manner so as to inspect the tumor grossly and rule out other types of obstructive pathologic change, such as cystic tumor or arachnoiditis, and then, in addition to suboccipital decompression, to uncap the lateral sinuses, the torcular Herophili and the occipital poles by means of section of the tentorium from the incisura to the lateral sinus. This procedure decompressed not only the posterior fossa anteriorly and posteriorly but the middle fossa as well by opening the dura over the occipital pole.

Clinical Data in Eight Cases of Cerebellar Medulloblastoma

Patient	Age, Years	Postoperative Irradiation	Total Number of Roentgen Units	Period of Survival, Months	End-Result
A. Treatment with Suboccipital Decompression and Irradiation					
R. B.	4½	3 series of 1,000 roentgens each	3,000	38	Excellent; attends school
R. McD.	12	1 series (?).....	?	20	Died
F. H.	17	4 series of 800 roentgens each	3,200	23	Died
M. W.	1½	No decompression; 1 series of 500 roentgens	500	3	Died
B. Treatment with Suboccipital Decompression, Tentorial Section and Irradiation					
M. M.	6	4 series of 1,000 roentgens each	4,000	46	Excellent; attends school
J. B.	17	3 series of 800, 1,000 and 1,000 roentgens, respectively	2,800	40	Excellent; is working
L. P.	4½	3 series of 900, 1,000 and 1,000 roentgens, respectively	2,900	38	Excellent; attends school
J. H.	9	2 series of 1,500 roentgens each	3,000	9	Very good; attends special school

The postoperative results were surprising not only in the prompt and great relief from intracranial pressure accomplished by freeing the cerebellum but in the fact that the patients manifested slight postoperative reaction to this procedure, which was in marked contrast to the usual increase in the temperature and the pulse and respiration rates observed in the first group of patients with decompression of the posterior fossa group alone. Dr. Chamberlain carried out a full series of treatments without disturbing reactions in intracranial pressure. All the patients are living and well today; the first patient in the series to be treated with suboccipital and tentorial decompression combined with radiation has passed the forty-sixth month and is still free from symptoms, attends school and is apparently normal. The tumor has not been surgically disturbed, nor has the cerebellar tissue been incised or extirpated in any of these cases.

I recognize the argument which may be advanced that in these cases the diagnosis of tumor of the tissue was not verified, but I believe that on the basis of the typical history and the presence of choked disk, with careful gross inspection of the cerebellum at operation, the type of lesion may be confirmed with a high degree of certainty. Both the response to high voltage radiation and the lack of mortality in this series offer proof in favor of the method adopted. Ultimate confirmation of the lesions will eventually be possible if these patients return for further relief. The children in this group have survived free from symptoms

far beyond the period for the series of patients with the usual treatment, and the operative risk has been greatly reduced by leaving the tumor alone.

Dr. B. J. Alpers and I are observing a case in which clinical evidence indicates that the child has a cerebellar medulloblastoma and in which high voltage roentgen therapy alone has brought about rapid improvement, recession of the choked disk and relief from symptoms. The therapeutic test employed by Dr. Sosman helps to confirm our diagnosis in this instance, and operative intervention may be delayed until an appropriate occasion.

There is strong evidence in this series, as in that of Sosman's, that high voltage irradiation is the method of choice in the treatment for cerebellar medulloblastoma. The neurosurgeon should provide adequate decompression in order to permit the roentgenologist full opportunity to deal with the lesion, and the neurosurgeon should base his choice of the method of relief on this factor as well as on consideration of the protection of vision rather than make a direct attack on the lesion per se.

DISCUSSION

DR. TEMPLE FAY: The question of not treating the tumor surgically is important. I have seen cases in which operation only jeopardized life. I have been impressed by certain specimens that Dr. Cushing presented—so extensive that surgical treatment failed to reach the major portion of the tumor. Because of the high mortality I have long wondered whether the surgeon did any good. In Dr. Cushing's series a life span of one or two years is shown after operation. My attitude has been that if there is any help in irradiation and the safety of the patient depends on my cutting the tentorium without disturbing the tumor, it is best to leave the tumor alone. As the tumor continues to grow with or without surgical intervention and irradiation, I think that the patient survives longer because there is more room for the growth.

As to treatment, we have a method by which Dr. Chamberlain gives small doses of radiation over an interval of from ten days to two weeks, then repeats the series in the third month and again three months later. Usually after the third series the patient was free from symptoms. I have continued to give high voltage radiation at intervals of three months, for the patient may live two years or more before signs of the tumor are again shown.

The low mortality in this series is evidence that one can obtain clinical relief without attacking the tumor. We have been struck with the fact that the usual postoperative reaction with tentorial decompression has been slight. The temperature has not risen above 101 F. in these cases, whereas formerly sharp reactions were frequent. I think that is another argument for leaving the tumor alone. We are perhaps unscientific in not obtaining tissue for verification, but I think the results are much better than we ever had before; when the characteristics of a tumor of this type were obvious, both clinically and grossly, securing tissue satisfied only an academic interest, at great risk to the patient.

A STUDY OF INVOLVEMENT OF THE AUTONOMIC NERVOUS SYSTEM IN LESIONS OF THE MIDBRAIN AND HYPOTHALAMUS, WITH POSSIBLE RELATIONSHIP TO PEPTIC ULCER. DR. HERBERT FREED.

Crile stated that peptic ulcer may well be called a wound stripe of civilization. It occurs rarely, if at all, in animals spontaneously; its incidence follows the rise of man in civilization. Incidentally, it not only favors the human race but is even selective in its victims and has its highest incidence in the medical profession.

Cushing advanced data in support of a theory that the neural portion of the hypophysis plays a rôle in the function of the parasympathetic nervous system comparable to that of the adrenal medulla in the function of the sympathetic nervous system. From this center, he said, fiber tracts pass backward to relay with the cranio-autonomic stations of the midbrain and medulla, of which the vagal nucleus is the most important. Experimental lesions anywhere in the

intracranial course of these tracts from nuclei to vagal center, presumably due to parasympathetic stimulation, are likely to cause gastric erosion, perforation, etc. Intracranial injuries and diseases affecting these same basilar regions of the brain are known to be accompanied by ulcerative lesions of the upper portion of the alimentary canal. Cushing suggested that vagal stimulation, by causing hypersecretion, hyperchlorhydria, hypermotility and hypertonicity, results in spasmodic contractions of the musculature, possibly supplemented by accompanying local spasms of the terminal blood vessels. Small areas of ischemia or hemorrhagic infarction are produced, the overlying mucosa being exposed to the digestive effects of its own hyperacid juices. The latest work, which is apparently of great significance, is that of the English workers Dodds, Noble, Hill and Williams (*Lancet* **1**:1099-1100, 1935). Dodds and his colleagues reported that they had prepared an extract in acetone and tri-nitrophenol of the posterior lobe of the pituitary which when injected subcutaneously into animals produces an acute hemorrhagic lesion of the acid-bearing portion of the stomach. The same effects can be produced in rabbits by the oral administration of extract. It has been shown that if the gastric contents are rendered alkaline prior to injection it is impossible to obtain the characteristic reaction. The most significant points concerning the gastric lesions are the extremely accurate limitation to the area of the stomach in which acid cells are present and the complete absence of lesions in other parts of the alimentary canal. Similar lesions have been produced in all animals tested, from the monkey to the mouse.

Dodds and his associates reported further that by repeated injections they produced ulcers which are analogous to chronic ulcer in man. Furthermore, they produced a temporary inhibition of secretion of hydrochloric acid, so that there was a temporary period refractory to histamine lasting six hours. Finally, they noted concurrent anemia, with depression of red cells from 6,000,000 to 1,000,000 and reticulocytosis up to 50 per cent.

That these results were not due simply to tissue extract was proved by the failure of any other types of tissue to give similar results. That the effects were not due to the oxytocic principle was shown by the fact that extract of oxytocic substance from 700 Gm. of tissue was not as effective as that from 1 Gm. of tissue containing the new principle.

Watts and Fulton (*Ann. Surg.* **101**:363-372, 1935) concluded that their experiments on 17 monkeys indicated no relationship between the destruction of any single group of hypothalamic nuclei and the changes in the gastro-intestinal tract; however, in every animal except 1 in which erosions of the alimentary canal were present a large hypothalamic lesion had been made; so it appears that large lesions in any part of the hypothalamus in monkeys may result in mucosal erosion or even in perforation of the upper part of the gastro-intestinal tract.

Grant reported 2 cases of lesions of the midbrain associated with peptic ulcer and suggested that in the first case the lesion may have involved the posterior hypothalamic nuclei and in the second the efferent fibers running from the nuclei.

We wish to report the incidence of gastro-intestinal lesions in 28 patients with lesions involving the midbrain or hypothalamus or both on whom autopsy was performed; in 19 instances the lesion was a tumor, in 8 of degenerative character and in 1 an aneurysm.

Furthermore, in contrast to these values we present the statistics of the frequency of cerebral lesions in a series of 175 cases of peptic ulcer (acute, chronic, healed and perforated) in which autopsy was performed between the years 1921 and 1935 at the Philadelphia General Hospital. In 27 of these cases necropsy was complete, including examination of the brain.

Of the first series of 28 cases, i. e., those in which lesions of the midbrain or hypothalamus were present, there was definite peptic ulcer in 5, in 2 of which the condition was acute, with perforation. In 1 case there were acute parenchymatous degeneration of the stomach and acute inflammation of the esophagus and larynx. These cases are summarized in the following table:

Clinical and Pathologic Data in Twenty-Eight Cases of Lesion of the Midbrain or Hypothalamus

Patient	Lesion in the Brain	Lesion of the Gastro-Intestinal Tract	Symptoms of Involvement of the Autonomic Nervous System
C. A.	Hemorrhagic glioma involving entire diencephalon and midbrain	None	Bulimia; hypertension; hypersomnolence; yawning
S. R.	Glioma of temporal lobe with compression of diencephalon and midbrain	None	Excessive salivation; hypersomnolence
D. S.	Hemorrhagic tumor in the midline	None	Epilepsy; diencephalic origin
J. D.	Glioma of temporal lobe with involvement of midbrain	None	Attack of sweating, hiccups and twitching of extremities
B. S.	Glioma of temporal lobe with involvement of midbrain	None	None
E. K.	Glioma involving thalamus and posterior limb of corpus callosum with destruction of posterior commissure due to pressure	Submucosal hemorrhage	None
H. J.	Glioma of left temporal lobe with gliosis and involvement of hypothalamus due to pressure	None	None
H. F.	Glioma involving posterior portion of corpus callosum with necrosis of posterior commissure due to pressure	None	None
N. S.	Frontoparietal glioma with involvement of basal ganglia and outpouching of third ventricle	Acute ulceration with perforation at cardiac end of stomach; acute ulceration of cardiac end of esophagus	Vomiting at very early stage; pupils fixed to light
F. K.	Bilateral frontotemporal glioma with pressure atrophy of diencephalon	None	Sleeping; yawning; Argyll Robertson pupils; hyperglycemia
V. L.	Craniopharyngioma arising from from pars intermedia of pituitary	Autolysis of gastric mucosa (post mortem ?)	Pupils unequal and almost fixed; yawning
A. W.	Capillary angioma of tuber cinereum	None	Somnolence; pyrexia without systemic infection
E. Q.	Pituitary tumor with pressure atrophy of tuber cinereum	Chronic gastric ulcer with hemorrhage	None
N. W.	Large chromophobic cell adenoma, with compression in region of tuber cinereum	None	Hypersomnolence; yawning
M. M.	Chromophobic cell adenoma	Acute inflammation of esophagus; acute parenchymatous degeneration of mucosa of stomach	Obesity
R. McD.	Chromophobic cell adenoma	None	Obesity
R. H.	Chromophobic cell adenoma	Submucosal petechial hemorrhages	Obesity; pupils fixed to light; polydipsia; increased sugar tolerance; "falling spells," preceded by general tremor and followed by sweating
N. W.	Basophilic cell adenoma and degeneration of posterior lobe of pituitary	Healed duodenal ulcer	None
G. Mc.	Colloid mass, replacing one half of posterior lobe of pituitary	Acute perforating ulcer	None
T. A.	Thrombotic aneurysm of circle of Willis with pressure atrophy of tuber cinereum	None	None
M. N.	Degenerative changes in nuclei of tuber cinereum	Healed duodenal ulcer	Hypersomnolence; obesity
A. K.	Encephalitic involvement of diencephalon (clinical)	Staining of serosa	Obesity; hirsutism; amenorrhea; hypertension (?); hyperglycemia; epilepsy of diencephalic origin

Clinical and Pathologic Data in Twenty-Eight Cases of Lesion of the Midbrain or Hypothalamus—Continued

Patient	Lesion in the Brain	Lesion of the Gastro-Intestinal Tract	Symptoms of Involvement of the Autonomic Nervous System
J. C.	Cellular degeneration in diencephalon and vagal nuclei	None	Hypersomnolence; grimacing
R. F.	Wernicke's polioencephalitis	Chronic gastritis (alcoholic ?)	Persistent vomiting; obesity; hyperglycemia
H. K.	Wernicke's polioencephalitis	Extreme distention of stomach	None
J. W.	Wernicke's polioencephalitis	None	Coma; ophthalmoplegia
T. M.	Wernicke's polioencephalitis	Hypertrophic stenosing lesion of pylorus	Vomiting; pain in stomach
H. R.	Wernicke's polioencephalitis	None	Persistent vomiting; semistupor; hyperglycemia

Finally, we summarized the cerebral pathologic observations on the 27 brains examined in the 175 cases of peptic ulcer listed in the files of the Philadelphia General Hospital. Of these 27 brains, only 10 presented cerebral pathologic changes of any degree. In 4 of the 10 cerebral arteriosclerosis was shown, and and in 2 others, meningitis. In these 2 cases multiple acute ulcers of the stomach were present; this is interesting in view of Rokitansky's description in 1859 of "softening of the stomach." One form which he described occurred "both in children and adults as a sequela of acute affections of the brain and its membranes, and more especially of tubercular meningitis at the base of the brain." Masten and Bunts (Neurogenic Erosions and Perforations of the Stomach and Esophagus in Cerebral Lesions, *Arch. Int. Med.* **54**:916-930 [Dec.] 1934) noted this and reported 6 cases of perforation of the stomach and esophagus associated with various cerebral lesions, 1 of which was meningitis terminal to abscess of the frontal lobe. In the same article these authors reported cases of intraventricular hemorrhage associated with perforation of the esophagus. In 1 of the cases in our series also intraventricular hemorrhage was associated with multiple acute ulcers of the stomach. This bears noting in view of the work of Keller, Hare and D'Amour, who experimentally produced lesions in the brain stem of 40 dogs and 50 cats and observed that "apart from 3 chronic mid-brain cats in which erosions were found in the stomach, the changes in the stomach have followed lesions accompanied by hemorrhage into the ventricles or transverse lesions at the level of the chiasm, unassociated with intraventricular hemorrhage."

In the remaining 2 cases peptic ulcer was associated with cerebral thrombosis.

Conclusions.—Twenty-eight cases of lesion in hypothalamus or midbrain or both are described, in 6 of which pathologic changes of the gastro-intestinal tract were presented. In 18 of these 28 cases symptoms of direct involvement of the autonomic nervous system were observed. One hundred and seventy-five cases of peptic ulcer were reviewed, and the cerebral changes were noted in 28 cases in which the brain was examined.

The reports, experimental and clinical, by the many workers in the field suggest the so-called neurogenic basis of peptic ulcer and indicate the need for complete autopsy in every case of peptic ulcer.

DISCUSSION

DR. HELENA RIGGS: I wish to show some microscopic slides later. In the case of the boy with acute perforation of a gastric ulcer the diencephalon presented no gross lesion, but the pituitary showed a large colloid mass, apparently an enormously distended cyst in the pars intermedia. If one analyzes this case according to the theory of the English workers Dr. Freed quoted, one would

consider this colloid mass as a storage of excessive amounts of the hormone of the posterior lobe, which had a specific effect in increasing peristalsis in the stomach. As result of this excessive stimulation, there was formation of acute ulcer with perforation.

An interesting observation in the pituitary gland in this case was the presence of a mild but diffuse proliferation of basophilic cells in the anterior lobe. These cells were large and were filled with heavy granules, suggesting physiologic activity. What part, if any, this basophilic proliferation played in the production of acute ulcer I am not able to say.

DR. TEMPLE FAY: I recall the case of a patient who died. He began to vomit coffee-ground material. At autopsy many small ulcerations were observed. In another case, while I was attempting to free a pituitary tumor, the patient vomited coffee-ground material. I know that the acute manifestations of gastric ulcer may follow trauma to the infundibular area.

OBJECTIVE SYMPTOMS OF INVOLVEMENT OF THE SPINAL CORD IN CASES OF PERNICIOUS ANEMIA REMOVED WITH TREATMENT. DR. SAMUEL B. HADDEN and DR. GEORGE WILSON.

There is considerable difference of opinion as to how much the symptoms of involvement of the cord in cases of pernicious anemia may be influenced with treatment, but all are in agreement that the advanced sclerotic changes cannot be influenced. We believe that not all the symptoms of involvement of the spinal cord associated with pernicious anemia are the result of sclerotic processes but that many are due to changes which precede sclerosis; these, we believe, can be definitely influenced with treatment even after they have been present for some time. Edema of the cord probably accounts for these symptoms.

CASE 1.—The patient was first seen fourteen months after the onset of the illness and presented well established posterolateral sclerosis, with practically complete loss of power in the lower extremities. Two years later the patient was able to walk unassisted but had a mildly spastic gait. Sense of position was lost below the hips.

CASE 2.—The patient was seen two years after the onset, when there was marked ataxia in all extremities, with loss of sense of position in the toes and impairment in the fingers. Vibratory sense was lost below the knees and was impaired in the hands. There was astereognosis in both hands, with inability to write or button the clothes. The knee jerk was present bilaterally, but the achilles jerk was absent; the Babinski sign was present on both sides. Eighteen months after treatment all tendon reflexes were normal, and plantar stimulation produced normal responses. Vibratory sensation was still lost below the knees, but perception of vibration and position and stereognosis were normal in the hands. Writing and use of the hands were also normal.

CASE 3.—The patient was first seen three months after the onset, when there was ataxia in all four extremities, with astereognosis and loss of ability to write. Sensation of position was greatly impaired in the hands and feet. Vibratory sensation was lost below the knees; the knee and achilles reflexes were increased, and there was ankle clonus on both sides. The plantar reflex was normal. After eight months of treatment station and gait improved. Sense of position and stereognosis were normal. Vibratory sensation was present throughout the body but was impaired below the knee.

CASE 4.—The patient was first seen three years after the diagnosis of pernicious anemia was established and about seven months after the onset of symptoms of involvement of the cord. The patient had discontinued liver therapy about a year earlier but had taken an adequate supply of liver extract for seven weeks before the first examination, when she was unable to walk without support on both sides. The gait was of a tabetic type, and the patellar reflex was absent on both sides. The patient was unable to recognize position or vibration in the lower extremities, and in the hands there were impairment of vibration and loss of

sense of position and stereognostic perception. The Babinski sign was present bilaterally. The lower extremities were hypotonic. Four months after treatment the patient was able to walk with a mildly ataxic gait and was then able to perform all her household duties. There was mild impairment of vibratory sensation below the knees. Stereognosis was normal, and she was then able to crochet. Two months later the patellar reflex was first obtained and gradually increased to moderate exaggeration. The plantar reflex is now normal on both sides, and the tonus in the lower extremities is slightly increased.

Comment.—In all these cases disappearance or marked diminution in many objective signs of involvement of the cord was noted, even in cases in which the disease was of two years' duration. The treatment consisted of administration of very large doses of liver extract, iron, copper and hydrochloric acid; vitamins A, B and D and fresh air and sunshine were used freely. In our experience, the objective symptoms of involvement of the cord in association with pernicious anemia can be influenced by vigorous treatment.

DISCUSSION

DR. J. C. YASKIN: I can hardly boast of the recoveries which Dr. Hadden and Dr. Wilson reported, but I think it would be worth while to mention two or three cases in my experience. One was that of a very thin, pale young man, a chair patient for two or three years at the Philadelphia General Hospital, whose condition was diagnosed as paraplegia. Special investigations discovered that he had severe anemia due to infestation by Diphyllobothrium. Removal of the cause and use of an antianemic diet resulted in complete recovery, with return to full duty.

A woman aged about 35, with good nutrition and color, was referred to the hospital with a diagnosis of arthritis and neuritis. Neurologic examination showed evidences of marked posterolateral sclerosis, with inability to walk without assistance. Examination of the blood gave conclusive evidence of pernicious anemia. With proper diet she improved sufficiently to do full duty as housewife and business woman. I have seen a number of other cases in which there was marked clinical improvement, but in relatively few instances did the pathologic signs, such as the Babinski reflex, disappear. On the other hand, in the majority of cases of advanced disease no improvement is shown, in spite of the amount of treatment. This is particularly true in cases in which there are complications, such as bed sores or cystitis and pyelitis. As was pointed out in a recent article by Dr. Strauss and his co-workers (Strauss, M. B.; Solomon, P.; Schneider, A. J., and Patek, A. J.: Subacute Combined Degeneration of the Spinal Cord in Pernicious Anemia, *J. A. M. A.* **104**:1587-1592 [May 4] 1935), the degree of improvement often depends on the energy with which the treatment is pushed. In addition to the specific treatment for anemia the general hygienic condition of the patient must be thought of at all times. Lastly, I think that even though one cannot produce cure in cases of involvement of the spinal cord due to pernicious anemia a great deal can be done to arrest the degenerative process of the central nervous system.

DR. F. H. LEAVITT: Some years ago I saw a patient with a posterolateral sclerosis syndrome associated with pernicious anemia of long duration. The symptoms of disturbance in the cord had lasted from two to three years, despite the usually accepted type of therapy. No improvement occurred in the neurologic condition until there developed an acute febrile illness which was diagnosed as "intestinal flu." At that time the patient was extremely ill and had a high temperature for several days. A few weeks after the termination of this acute intercurrent illness, she began to improve, and the improvement continued so that she is now able to get out of bed and walk by herself; many of the symptoms of involvement of the posterior and lateral columns of the cord have disappeared. This is the only case I have observed in which an intercurrent febrile infection produced marked amelioration and later improvement in the posterolateral cord syndrome associated with pernicious anemia.

DR. HELENA RIGGS: In the early stages of primary pernicious anemia there may be edema of the cord analogous to that in the extremities. In such cases edema impairs function but does not destroy cells, and as the red cell count increases and edema disappears function may be reestablished.

DR. W. E. ROBERTSON: What was the duration of most of the symptoms?

DR. S. HADDEN: Two years.

DR. W. E. ROBERTSON: I am convinced that a more definite diagnosis would be possible in the cases referred to by Dr. Yaskin if a study were made of the gastric contents, because total achylia is consistently the rule. Dr. Minot once said to me that he had never observed a typical and unequivocal case of pernicious anemia in which total achylia was not shown. The objective findings of macrocytic anemia, high volume index and total achylia and, in the vast majority of instances, punctate hemorrhages in the eyegrounds, when linked with the subjective phenomena elicited from the patient, bespeak pernicious anemia. Then, too, in these cases there is rapid emptying of the stomach, which may readily be seen fluoroscopically. Further confirmation is obtained when liver is administered. Reticulocytosis occurs, with the count in inverse proportion to the red cell count. It is possible also to determine the most appropriate liver therapy by means of a reticulocyte count. If these cells to which Cesaris-Demel first called attention, continue to manifest a cycle of response after administration of various forms and amounts of liver, full efficiency has not been reached. The use of hydrochloric acid has been of value in some forms of anemia, but prior to the advent of liver therapy it never exercized any influence on pernicious anemia. It often adds, however, to the comfort of a patient with pernicious anemia during the early stages of liver therapy.

Appropriate measures make possible the recognition of primary pernicious anemia long before any nervous condition develops. Lack of care in diagnosis, carelessness on the part of the patient or inability to procure appropriate therapy for economic reasons are responsible for complications of involvement of the nervous system. Even in cases of advanced disease in which involvement of the nervous system is definite, complete recovery may be possible if appropriate doses of liver are employed, as determined by the degree of reticulocytosis. The achylia gastrica is a fixture in any event.

DR. ROBERT MATTHEWS: I wish to ask if any correlation was found between the blood count and the improvement in symptoms? Was it necessary to bring the red cells up to 4,000,000 before the neurologic picture improved?

DR. SAMUEL HADDEN: There was no constant correlation. Several patients seemed to improve in proportion to the increase in the blood count, but the last of the cases reported is of considerable interest because when the patient was first observed the hemoglobin was 95 per cent and the red cell count 4,200,000. She had been treated with liver for two years and had discontinued its use seven or eight months prior to the onset of the neurologic symptoms; she had resumed the liver about a week before she was first observed. Her blood count was apparently satisfactory during the time when the symptoms were developing, and there is little doubt that this is frequently the case. In most instances, however, there was no neurologic improvement until the blood picture began to approach the normal.

We wish to make it clear that we do not imply that in all cases posterolateral sclerosis due to pernicious anemia can be favorably influenced. These cases were selected because of the disappearance of definite objective symptoms.

Dr. Yaskin's comment on the cases in which the condition closely resembles posterolateral sclerosis and pernicious anemia does not exist is of interest. All have seen these instances, and I believe that in many the disease is based on a vitamin deficiency. At least, in many instances the patient has improved with vitamin therapy. Our experience has convinced us that the addition of iron and vitamins A, B and D are of benefit in the management of posterolateral sclerosis.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Dec. 19, 1935

C. A. McDONALD, M.D., *Presiding*

EFFECT OF EXPERIMENTAL LESIONS OF THE CORTEX ON THE PSYCHOGALVANIC REFLEX. DR. HENRY G. SCHWARTZ.

This article will be published in full in a later issue of the ARCHIVES.

THE FALLING SICKNESS, OR AN ADVENTURE IN BOOK COLLECTING. DR. WILLIAM G. LENNOX.

As a result of the stimulating interest of Dr. Theodore J. C. Von Storch and with the aid of a grant from the Milton Fund of Harvard University, I undertook the accumulation of all available writings on the subject of epilepsy. The enterprise has had two phases: the translation of previously untranslated incunabula and the collection of old books.

For the incunabula we have depended on Mr. Ballard of the Boston Medical Library, and the translation was done by the Reverend Father English, O.P., an expert in this field. The authors whose writings on epilepsy have been translated and the dates of publication are as follows: Arnold of Villanova, 1482; Anthony Guianerius, 1488; William of Saliceto, 1490; Bernard Gordon, 1491; John of Gaddesden, 1492; Serapion Sr., 1497, and Hugh of Sienna, 1498.

We have to date accumulated 45 books on epilepsy. The earliest was printed in 1617, and two thirds of the number were published before 1900. By means of quotations from these publications, the development of thought concerning the cause of epileptic seizures and their treatment can be traced.

RESULTS OF TREATMENT OF DEMENTIA PARALYTICA WITH FEVER INDUCED BY DIATHERMY. DR. SAMUEL H. EPSTEIN, DR. HARRY C. SOLOMON and DR. I. KOPP.

A review of the literature on the results of treatment for dementia paralytica with fever produced by diathermy and related mechanical modes of hyperpyrexia shows that of a total of 648 cases, reported between 1929 and 1935, good remissions were secured in 27 per cent. We present the results in a series of 33 cases in which treatment with diathermy was carried out in the Boston Psychopathic Hospital between February 1931 and February 1934, with an analysis as of February 1935. Some patients received other treatment as well, prior to or subsequent to the treatment with diathermy. According to our analysis, 8 patients were improved and were working, and 7 were improved but were not self-supporting. Four patients, though remaining hospitalized, were known to be improved. Four patients were living but were not improved, and 10 patients had died. In 1 patient of the total series there was a definite clinical relapse and reversion to a positive serologic reaction four years after diathermic fever therapy.

There appeared to be a definite correlation between the clinical status and the reaction of the spinal fluid in the cases in this series. Of the 15 patients who were clinically improved 8, or approximately one half, had a normal or nearly normal reaction of the spinal fluid. No adequate figures are available in the literature on the reactions of the spinal fluid after diathermy treatment. In our series of 33 cases it is estimated that in 22 per cent of the cases there was a normal reaction of the spinal fluid after treatment.

With regard to the duration and degree of fever productive of the best therapeutic results, it is not possible from our experience to draw any hard and fast conclusions. It is quite possible, however, that our results in the total group of cases would have been much better if the diathermy treatment had been more prolonged and a higher level of temperature had been maintained.

Ten patients of the series died, and in all but 1 case death occurred within one and one-half years. These patients showed no clinical improvement and no appreciable improvement in the response of the spinal fluid before death. The causes of death indicate that the disease was active in at least 9 of the 10 cases. Longevity figures, based on the percentage of patients who died within two years after treatment, indicate that 27 per cent of the series of patients who were treated with diathermy died within two years after treatment. This value may be compared with the previously reported figures of 14.8 per cent for the series in which malaria treatment was given and 13.5 per cent for the series in which tryparsamide was administered.

A table of data is given comparing the clinical results obtained in patients treated with malaria, artificial hyperpyrexia, including diathermy, and tryparsamide. This shows that the best remissions were obtained in a little over 45 per cent of the patients treated with malaria and in 42 per cent of the patients treated with tryparsamide, as compared with 27 per cent of the patients treated with artificial hyperpyrexia. A comparative study of the serologic results in our series of cases indicated that in about 22 per cent of the series in which diathermy was used a normal reaction of the spinal fluid was shown, as compared with 37 per cent obtained for both the series in which treatment with malaria was given and that in which tryparsamide was administered.

In our experience in the treatment of dementia paralytica, better results have been obtained with the use of malaria and tryparsamide than with that of diathermy. However, it is to be emphasized that with the use of a greater amount of artificial fever the results might have been somewhat improved.

NEW YORK NEUROLOGICAL SOCIETY

Dec. 3, 1935

ISRAEL WECHSLER, M.D.

President, Presiding

LYMPHORRHAGIA RETINALIS TRAUMATICA. DR. NATHAN SAVITSKY and DR. SIDNEY W. GROSS.

A case of lymphorrhagia retinalis traumatica (Purtscher) is described, in order to call this clinical problem to the attention of neurologists. Up to the present all cases have been investigated and reported by ophthalmologists. No pathologic study has been recorded. Anatomic studies of the affected eye in the present case are now in progress.

A man aged 75 was struck by an automobile on Sept. 20, 1935. The question whether he was unconscious could not be settled. He was admitted to the Morrisania City Hospital on that day, and a laceration of the parietotemporal region of the scalp was sutured. He left soon afterward, against advice. When he reached home he became drowsy and confused, and he was brought back to the hospital on September 22. On that day examination revealed a scalp wound in the parietotemporal region, hematoma and ecchymosis behind the right ear and superficial bruises in the region of the right shoulder and in the iliac region on both sides. The blood pressure was 150 systolic and 70 diastolic. There was right hemiparesis. Speech was incomprehensible. The Babinski toe sign was present on the right, and the abdominal reflexes were diminished on both sides. Examination of the spinal fluid on September 29 revealed a pressure of 6 mm., no block, xanthochromia and 850 red cells. No organisms were grown on culture. Wassermann tests of the blood and spinal fluid gave negative reactions.

The urea nitrogen content was 41 mg. per hundred cubic centimeters of blood. The patient was unable to give an account of his past life. The signs on the right side and aphasia, marked confusion and fatuous euphoria persisted; a few days before death the patient became more disturbed and restless. He died of bronchopneumonia on Oct. 11, 1935.

Examination of the fundi showed mild retinal arteriosclerosis on the left. The right fundus showed many small bright, white round spots; they were especially numerous in the peripheral and inferior portions. The individual dots varied in size, the average diameter being about equal to that of the larger retinal vessels. At times the white dots became confluent to form larger white masses of irregular contour. These spots were apparently in the superficial layers of the retina, as they appeared to lie on the vessels and the larger masses seemed to pass over adjacent retinal vessels. The dots followed the inferior vein in a definite manner; otherwise there was no direct relation to the blood vessels. There was slight arteriosclerosis. The superior temporal and inferior nasal veins were slightly dilated. No hemorrhages were seen, but there may have been hemorrhagic extravasation beneath the mass of white spots in the periphery. The disk was obscured. The foveal reflex was absent. A gray murkiness was observed in the region of the disk, which contrasted strikingly with the shining, silvery spots noted over the retina. Vision could not be tested. The pupils were equal and regular and reacted sluggishly to light. Accommodation could not be tested.

Autopsy showed subarachnoid hemorrhages, especially in the right parietal region, and extensive laceration of the middle and inferior temporal convolutions on the left. The right eye was obtained for examination. Complete pathologic studies will be presented at a later date. Sections showed round structures within the retinal layers which reacted to the stain for fat. These bodies were somewhat more numerous in the superficial layers. The pathologic basis of this unusual retinal affection is still obscure. Most investigators agree that the white masses in the retina are probably due to lymph mingling freely with retinal elements. The sudden increase in intracranial pressure immediately after injury to the head is said to result in the breaking down of the walls of the perivascular lymph spaces.

DISCUSSION

DR. S. P. GOODHEART: This is an unusual contribution; I do not think that many have seen cases of this sort; it is the first in my experience. I saw the patient at the Morrisania City Hospital; there was some difference of opinion in regard to the diagnosis. The ophthalmologists thought that the case was one of retinitis albicans, but I think that this possibility can be excluded, for retinitis albicans affects both eyes and the appearance is different. Indeed, if there is any connection between the lesion in this case and trauma, retinitis albicans can be ruled out, as I believe that the latter disease is never the result of trauma. The case emphasizes the importance of the relationship between the neurologist and the ophthalmologist. The ophthalmoscopic picture is important in most cases of trauma to the head, not only for diagnosis but for prognosis and treatment. Lymphorrhagia retinalis traumatica has escaped the attention of most observers because of its rarity. Much study is needed to make a correct diagnosis in this unique condition. It does not belong to any of the ordinary retinal disturbances, such as albuminuric retinitis, but it resembles some retinal changes observed in association with diabetes. An important consideration is the relationship of this condition to commotio retinae, described by Berlin, and it is of theoretical and practical importance to know whether the two are identical. I believe that there is little relationship and that the pathologic picture is different in the two conditions.

A few weeks ago, at the Morrisania Hospital, my associates and I observed a young woman who had been struck on the head by a bottle that had fallen a number of stories. A fracture of the sphenoid bone, which indirectly affected the eyeball, was suspected. With the ophthalmoscope one saw definite edema of

the retina—a picture that looked much like that in this case—but without the spots which characterize Purtscher's disease. To me it resembled the picture in commotio retinae. It would be desirable if one could learn the pathologic changes in this condition. It is a question whether the small spots are really fat. I am impressed with that possibility for two reasons: First, in a series of cases reported in 1934 in which trauma had occurred, there were fractures of some of the long bones, and fat emboli in the lungs and important changes in the retina were observed. In 7 of the cases reported 3 autopsies were performed, and an examination of the retina was made. The changes in the retinal picture suggested a condition analogous to that present in the lung; in other words the, question arises whether the feature of the retinal pathologic change is fat embolism. The pathologist, Dr. Davison, has observed fatty changes in the retina. It will be of interest to know the nature of the small spots seen in the retina in a case of Purtscher's lymphorrhagia. It should be difficult to determine the underlying pathologic condition, since after death the retina undergoes immediate change. In the living subject the retina is translucent; immediately after death opacity occurs. It would be desirable if Dr. Savitsky and Dr. Gross were to determine how much the finer structures of the retina—the rods and cones—are involved. I incline strongly to Purtscher's theory: that the retinal changes are brought about by sudden change in intracranial pressure, in much the same way as choked disk is produced. The rapidity of the appearance of this condition after trauma makes it, of course, unlike choked disk. Probably lymphorrhagia is brought about by the concussion affecting the retina itself, with dilatation of the veins and capillaries. The picture shown in this case, in which the deposits follow the vein, suggests that cause strongly. On the other hand, since the lymphatics in the retina are deep seated, it is surprising that these spots are as superficial as they seem to be.

LIGATION OF THE COMMON CAROTID ARTERY: CLINICAL PICTURE AND ENCEPHALOGRAPHIC STUDY IN A CASE EIGHT YEARS LATER. DR. HERMAN WORTIS (by invitation).

Since Benjamin Travers first ligated the common carotid artery in the treatment of pulsating exophthalmos this condition and its treatment have continued to interest physicians. Various therapeutic measures have been reported by Dandy, Matas, Kolodny, de Schweinitz, Holloway, Fuchs and others.

In the following case the condition is of interest because it demonstrates in a graphic manner the damage to the brain which may result from ligation of the common carotid artery.

N. Q., a trained nurse aged 57, entered the Bellevue Hospital on July 27, 1935, in a disturbed state. She was confused and disoriented as to time and place and showed gross defects of memory and intellect; her condition was such as to make adequate contact impossible. She was quieted with sedative medication, and the following history (furnished in great part by Dr. DeWayne Hallett) was obtained.

On Nov. 1, 1926, the patient had been in an automobile accident. Her head was bumped against the windshield; the only obvious injury was a laceration over the left eye. There was no loss of consciousness, and the patient was able to return to work. Twelve days later the left eye became discolored and began to protrude slightly. One month after the accident she began to complain of noises in the head; she said they were like the swish of waves on the shore. The patient became more and more irritable, saying that the noise in her head was driving her mad. Roentgenograms of the skull were reported to show nothing abnormal. She visited various specialists, none of whom was able to determine the cause of the patient's complaints. Sixty-three days after the accident the patient was seen by Dr. Hallett for the first time. He recognized the trouble as pulsating exophthalmos—probably due to traumatic aneurysm of the carotid artery and cavernous sinus. The following characteristic triad was noted: (1) The left eye could definitely be felt to pulsate when the slightest pressure was put on the eyeball, and there were (2) measurable exophthalmos of the left eye and

(3) a subjective and an objective bruit. The latter could be heard over the entire left side of the head. It was also noticed that the bruit stopped when the left internal carotid artery was compressed.

The patient was put to bed, and twenty-seven days later (ninety days after the accident), with the use of ether anesthesia, the left common carotid artery was ligated by Dr. George W. Roberts. The immediate effects were complete cessation of the bruit, right hemiplegia and total aphasia. Sensation was apparently not tested at that time. Fourteen days after the operation the bruit recurred, in a light blowing form, audible only at the outer angle of the left orbit. It ceased on compression of the carotid artery. On the one hundred and thirty-third day after the accident the left superior ophthalmic vein was ligated. After this second operation the bruit stopped, but vision began to diminish in the left eye so that by September 1927 she could perceive only light in that eye.

Neurologic examination at the time of her admission to the Bellevue Hospital revealed: about 3 mm. of exophthalmos in the left eye; left pupil larger than the right and reacting poorly to light on direct stimulation (its consensual reaction was good); left nerve head pure white; arterioles and veins of the left retina thin as compared with the vessels of the right; visual acuity 16/20 in the right eye; light perception only with the left eye; visual field of the right eye well within normal limits; right hemiparesis, including the lower part of the face, and associated muscular atrophy. The gait was typically hemiplegic. There was a downward drift of the outstretched right hand, which was markedly accentuated when the eyes were closed. The deep reflexes were overactive on the right, and the abdominal reflexes on that side were quickly exhausted. There was a Hoffmann sign but no Babinski toe sign on the right. Sensory examination revealed right hypesthesia and hypalgesia to all forms of sensation; this was most marked peripherally in a glove and stocking fashion. There was complete loss of sense of position on the right, with astereognosis in the right hand. Both right extremities showed trophic edematous changes, which were most marked peripherally. The spoken and the written word were understood perfectly. Speech was slow; when the patient became tired or confused there developed typical anomia, which was not present at any other time. No bruit could be heard anywhere over the head.

The psychiatric survey is of interest. The patient has shown marked intellectual impairment since the operation. She is no longer able to carry on her duties as a housewife and is almost completely dependent on her children. She has been picked up on street-cars, wandering aimlessly about, with complete amnesia. Her attitude toward her children has changed. She has become dictatorial and irritable. Her daughter states that the patient has attempted suicide on two occasions—"never with any serious intent but merely to attract attention to herself." Her mood during her stay in the hospital varied; at times she was cooperative and appreciative and at others given to fits of choleric temper controllable only by large doses of sedatives.

Laboratory Data.—The blood pressure was 135 systolic and 90 diastolic in both arms. Roentgenograms of the skull revealed nothing abnormal. A 6 foot (182.9 cm.) heart plate revealed slight dilatation of the left ventricle. Encephalograms revealed the typical unilateral hydrocephalus ex vacuo characteristic of degeneration of one cerebral hemisphere. The blood count revealed: red cells 4,900,000, hemoglobin 90 per cent and white cells 7,880, with a normal differential count. The nonprotein nitrogen content was 31 mg., sugar 87 mg., calcium 10.1 mg. and phosphorus 4 mg., per hundred cubic centimeters.

Summary.—This report is concerned with the neurologic and mental changes in a patient eight years after the ligation of the common carotid artery for the relief of pulsating exophthalmos (traumatic aneurysm of the carotid artery and cavernous sinus). The encephalographic study illustrates the degree of damage to the brain which may follow ligation of this artery.

In this case is demonstrated the danger of complete ligation of the common carotid artery without first encouraging the development of a collateral circulation by digital compression.

DISCUSSION

DR. GEORGE H. HYSLOP: I think the point made by Dr. Wortis is important—that if possible a preliminary period should be allowed in which collateral circulation may develop. I have seen a number of cases at the Memorial Hospital in which there were no untoward sequelae. A number of patients with malignant disease in the neck suffer a degree of compression of the carotid artery, which is the equivalent of a designed effort to encourage collateral circulation. I think that the encephalographic films reveal not merely the natural consequence of ligation of the common carotid artery but the effects of the associated thrombosis.

DR. RICHARD M. BRICKNER: Dr. Wortis' case is of additional interest in view of the partial loss of the cortex of one hemisphere which must have occurred. The literature contains the report of 1 case in which the entire right hemisphere was removed for the treatment of tumor (O'Brien, John D.: Removal of the Right Cerebral Hemisphere: A Case Report, *Ohio State M. J.* **28**:645, 1932). Dr. O'Brien, who performed the operation, found that sensory and motor function on the opposite side of the body returned in some degree. In that instance the corpus striatum and thalamus were left intact or nearly so, but in the case reported by Dr. Wortis these parts probably suffered considerable damage, and the explanation of the preservation of function is even less clear than in Dr. O'Brien's case. Cases in which the whole or a part of a hemisphere is lost are rare; it is to be hoped that Dr. Wortis will continue to observe the patient.

DR. HERMAN WORTIS: In 2 other cases of pulsating exophthalmos which were brought to my attention by Dr. King and Dr. Kennedy, the common carotid artery was ligated without any untoward result. In these cases, however, the collateral circulation to the ipsilateral hemisphere was encouraged by digital compression for forty-five minutes (which a patient can be trained to stand every three hours). Later the artery can be clamped.

In reply to Dr. Brickner's comment, a great deal of function was apparently taken over by the other side of the brain. Immediately after the operation the patient had hemiplegia and complete aphasia. At present she has hemiparesis and only occasionally sensory aphasia.

This case may be compared with that to which Dr. Brickner refers in which hemidecerebration was performed except that in the present case the occipital lobe apparently was spared, since the visual field of the right eye was well within normal limits.

COMBINED SYSTEM DISEASE IN TABES DORSALIS. DR. CHARLES DAVISON and DR. HAROLD KELMAN (by invitation).

This paper will be published in full in a later issue of the ARCHIVES.

RELATIONSHIP OF INTELLECT TO SPEECH IN PATIENTS WITH APHASIA, WITH ILLUSTRATIVE CASES. DR. FOSTER KENNEDY and DR. ALEXANDER WOLF (by invitation).

We have shown how functions concentrate their powers in the body, as, for example, in the dominance of the left hemisphere, and how the cortex of the left hemisphere is divided further into specific areas for speech. Lesions injuring these centers produce aphasia—a loss of symbols—which is quite distinct from any intellectual defect. Examples are cited demonstrating the retention of intelligence and thought in the presence of word loss. Although thought processes are frequently affected in persons with aphasia, especially those with large lesions, it is no more fitting to regard "mind" and speech as one than it is to expect every moron to have aphasia. Apraxia, until now looked on as a variant of aphasia and a defect in symbolism, we believe to be a sign of intellectual blemish. We have tried to build a concept of localization in disorders of speech the construction of which is secure and well rooted in the tradition of organic neurology and removed from what amounts to the mysticism of some modern schools. To us

the idea of centralization of the function of speech has been an aid in the study of physiologic function and in diagnosis, while our distinction between symbols and intellect has given us a respect and sympathy for the aphasic mind that may lead to greater understanding.

DISCUSSION

DR. FREDERICK TILNEY: It is true that the origin of aphasia has challenged every great neurologist. Dr. Kennedy looks on this difficult problem as a sort of fiddle on which one tests his neurologic acumen. Few have taken it up and played it with anything like the effectiveness with which it has been heard tonight. Personally, I can see why it is relatively easy for Dr. Kennedy to handle this subject. His own splendid gift of language gives him a peculiarly penetrating insight into the processes of speech. Some things which he has said should sink deeply into the minds of neurologists of the present, for it is regrettable that so many leaders have gone and their examples have been lost. Many of the things which they taught seem to have been forgotten.

First, there is the prevalent idea of speech as the result of the whole brain acting at once. This seems to me a lazy man's idea. I feel certain from what I know of the cortex that there is a degree of localization for speech concerning which there is no conception. The complexity of this localization challenges one to go back to the attitude of the forefathers in neurology. They worked diligently to produce interpretations of their clinical studies. An effort and an attitude of this sort remain for present day workers to pursue. The idea that speech and intellect are interdependent has gained a large following among modern thinkers. On the other hand, Dr. Kennedy has cited many cases in which evidence makes this proposition untenable.

A short time ago I read William Gladstone's "Juventus mundi." In this great analysis of the Iliad and the Odyssey, Gladstone set the age of Homer at about 1,100 B. C., considerably before the time of written speech, and thus made it clear that these great poems had been handed down through many hundreds of years by word of mouth. Those who have read either translations or the originals know what wonderful shades of meaning exist in the various combinations of words, not only in the rhythm and the swing of the meter but in the picturing of incidents and the delineation of character. It can seem no less than a marvelous achievement that the 30,000 lines of these poems were handed down through seven or eight centuries merely by the spoken word. To me it seems probable that, in many instances at least, the bards who passed on this work may have done so in a more or less mechanical way and not necessarily with much understanding of the contents, the music of the verse carrying them through without much reference to the intellectual interpretation.

Dr. Kennedy has asked me to say a few words about my personal experience in respect to aphasia. I do not know whether or not this will interest you, but it may have a bearing on the idea of cerebral dominance. First, it should be stated that I was born left handed. This interpretation seems fair from the fact that everything I did originally was done with the left hand. An old Irish nurse started in early to correct this left-handed tendency, with the hope of making me right handed. It was her custom to call me *kathoge*. This is an old Gaelic word; it means "a left-hander," and its implications of scorn and contempt could not fail to impress one with one's inferiority. This scornful appellation finally had its effect. When the time came for me to learn to write, it was my inclination to use the left hand, but this tendency was overcome by what was probably another good Gaelic custom, simply tying a stocking on the left hand and so compelling me to use the right. Eventually I did become a right-handed writer, but in everything else I was distinctly left handed; that is, I ate with my left hand and still do, a fact which makes me an uncomfortable neighbor at dinner. This habit was something which my kind Irish guardian and friend was never able to correct. I played tennis with my left hand and pitched ball in what is known as southpaw fashion. In a word, I ultimately exhibited a mixture of artificial ambidexterity, with great emphasis on the left side in skilled and learned performances.

When I suffered from what has been called a vascular accident there was, I am told, a short period of complete aphasia, and after that speech returned completely. At first and even now, when I am speaking in public I have the feeling that I am saying something wrong. It is a somewhat ghastly feeling. For a moment or so I lose that train of speech, a defect which seems to me to be due to the fact that there are interruptions in the internal hearing of speech, with loss of continuity in expression. Naturally, such interruption leads to confusion, making it difficult to continue along the line which is being developed or causing me completely to lose the thread of the argument. It requires some time to get back to the right groove and often necessitates starting over again and keeping a watchful ear on each spoken word. Usually by this means, together with a marked decrease in the rate of speech production, it is possible to take up again the train of thought. Writing with the right hand was and still is impossible. In time I began to realize the great degree of handicap imposed by this inability, and so I started to learn to write with my left hand. At present my handwriting is entirely left handed. At first I had difficulty in producing legible copy, but by a process of making simple lines and curves, I progressively acquired more facility, with a greater sense of naturalness in my left-handed writing.

Last summer I was surprised on one occasion, while telephoning, to observe that I had picked up a pencil with my right hand and again had attempted to write. I was unable to make any intelligible letters or figures, and almost immediately on observing what I was doing the power to write ceased. Numerous attempts have been made since to use the right hand again in writing, but the more energetically I concentrate in the effort the more difficult the act of writing becomes. The time elapsed since the acute attack is now over ten years.

I agree with Dr. Kennedy that it is a mistake to teach an absolutely left-handed person to be right handed. If I had been allowed to be completely left handed, as I started out to be, it would have been better. I also believe that handedness is in large measure a matter of stock. Heredity plays an important rôle. My grandfather on my mother's side was left handed, as was also my mother. In my own generation, in a family of 4 brothers, 2 are left handed, and my son has definite left-handed tendencies. I believe this trait has come down through the maternal side of my family, for my father and all the members of his family, so far as I can trace, were definitely right handed.

I think one must bear in mind the many words of wisdom which Dr. Kennedy has spoken tonight. One can apply this to oneself with redoubled force in the understanding of the function of speech. Some neurologists are of the opinion that today neurology is a completed chapter, a finished book. This cannot be true. A good understanding of the first chapters has scarcely been provided. As a discipline in the structure and physiologic aspects of the nervous system there are many valuable leads to be followed on the organic side. Neurologists would benefit themselves, as well as the subject of their chief interest, by eliminating much of the loose thinking which the purely psychologic attitude of the modern day has enforced.

Dr. George W. Henry (by invitation): I presume I represent that group of persons referred to as the mystics who are interested in modern neurology. I myself am primarily interested in the function of the brain as a whole, and in spite of that fact I agree with practically everything that Dr. Kennedy has presented. I do not think that any one who is acquainted with the point of view that I represent, that of studying the organism as a whole, of interest in the total function of the intellect, has quarrel with any one who wishes to study the specific functions of the parts included in this whole. Neurologists with my point of view are pleased with any progress in the study of aphasia, in the hope that the understanding of the whole may be in that way increased.

Dr. Kennedy did not explain that in his paper he used the word "mind" with quotation marks. I presume he did so because he did not take the term seriously. He uses the term intellect without quotation marks, and if he meant seriously to

use the word intellect in that way I cannot agree with him. "Mind" and "intellect" are reminiscent of the period in which spirits and similar concepts had considerable value. To me they have no scientific value. I do not understand how a person can seriously consider intellect—a pure abstraction—as having much scientific value. If Dr. Kennedy meant by this term intellectual function or something similar, I can follow him.

I am puzzled also by almost all the descriptions of aphasia in books and elsewhere—by the presentation of disorders as though they occurred in a purely mechanistic person entirely devoid of feeling. That brings me to my real comment on the presentation. I do not see how one can understand aphasia and really study it, or perceive the relationship of aphasic and intellectual disorders unless he includes consideration of the emotional disorders or the emotional component of aphasic disturbances. A patient not long ago told me that she deliberately did not try to speak after her attack because she was so embarrassed by the results of efforts to speak. In one of the cases which Dr. Kennedy described he made the notation that the patient was profoundly elated. It is impossible for a person to be profoundly elated without his intellectual functions being affected accordingly. In another case a boy did not speak; eighteen months later he was able to recall rather suddenly a scene he had observed but had not verbalized. I cannot understand that abrupt change except as a manifestation of emotional resistance to speaking. Certainly, there was no sudden change in the structure of this boy's brain, or probably not in any physiologic process. A rather important psychologic change had occurred at that time with respect to certain conditions, and he began to speak.

I am able to understand aphasic disorders much better if I try to trace the way in which speech has evolved. In the beginning (and I am not going into details) animals communicated with each other by making sounds that were associated with certain attitudes, and other animals understood the association of attitude and activity with these sounds. The child in the beginning makes sounds chiefly to express states of discomfort or pleasure. Later, these sounds became transformed into words, but what the child says is still chiefly expressive of his feelings, and so it goes until one comes to the person of the most intellectual type, who divorces as much as possible his personal feeling from what he has to say. I think that exactly the reverse takes place in aphasia and that on that account the person who is practically totally aphasic is able to blurt out things under impulse or emotional stress. He is able to express himself, when he cannot do the same thing by deliberate choice. There is a tremendous initial drive which makes it possible for what remains of his brain to function; it is not possible if he undertakes to do the same thing deliberately. This may be related to the tests that are used. It is commonly observed, and was noted tonight, that a person may do something spontaneously, but if he is requested or deliberately wants to do it, he is unable to perform the act. It seems, then, that there must be a connection between the person's embarrassment or his anxiety when somebody else asks him to do something and his ability or inability to perform. I think that the neurologist who is interested in these functions (that is, the purely intellectual and the purely aphasic function) has a great deal to contribute to this subject, and I do not understand how aphasia can be considered as it seems to be in this paper, as just a manifestation of a defect, when it must obviously be a manifestation of what it left, i. e., of the brain minus a part which is destroyed.

DR. PAUL SCHILDER: When I learned of aphasia in the study of physiology I formed a mental conception of the clinical picture which was very different from what I saw later in the clinic. The person with aphasia is not merely aphasic; he also shows decided changes in the structure of his personality. The two main types, motor and sensory, are indeed different personalities. The patient with motor aphasia is moody, does not like to talk, is withdrawn and lacks interest in other fields than that of speech. The patient with sensory aphasia is optimistic and full of joy and energy, with a great deal of impulse in his speech as well as in other ways. On the whole, he behaves almost in the same way as the patient

with postencephalitis. There is a change in the total personality. This change is due to a specific lesion. The patient not only is unable to do some things that the normal person can do; there is not only a defect in function but a totally different function of the personality. This formulation unites the two points of view which have been offered.

The question remains: What makes up the disturbance in speech of the patient with aphasia? I do not think that it is satisfactory to say that speech symbolizes thought. It is true that the term symbol is used in a different way. It is advisable to use this term only when there is an inner relation between the symbol and what is symbolized. In speech words and sentences function merely as signs and signals. These are in no way natural signs and have no inner relation to the object that is meant. With Ogden and Richards, I prefer to use the terms sign and signal for the word and sentence and the term referent for the object to which the sign points. One should, therefore, call aphasic disturbances not disorders of symbolic thinking but disturbances in the function of signals or signs. What is a signal? I refer here to the experimental work of Pavlov in which a sound or light signal is associated with the offering of food. The light or sound signifies an object (referent). The object which is announced by the signal is the meaning of the signal. The sign says: "Something must be expected." The subject to which the sign is directed comes into a state of expectation. This state is not only a psychic occurrence but an objective attitude which expresses itself in motility and in the vegetative system (salivation). The signal (sound or light) means: "Get prepared as an organism from the emotional, vegetative and motor point of view." If one considers what happens in the conditioned reflex he gets new help for the understanding of the function of speech. When an auditory condition reflex is formed, a sound of any wavelength is effective. Differentiation takes place by a process which can be compared to the process of trial and error. The sign is at first a general one; by the process of experimentation it becomes a more specific signal. Finally, the dog reacts only to a sign of definite wavelength.

The same process takes place in the development of language. A child may hear the word uncle when an elderly person approaches. The sign may at first mean every elderly person—later, a man—still later, a man who is kind and brings candy—finally, a specific person. The logical insight into the meaning of the word uncle is the product of a complicated mental development. Experimental processes are continually going on concerning the validity of the sign function. The sign becomes the more reliable the farther the experimentation has progressed. When the sign function is disturbed the sign becomes incorrect and unreliable. In cases of aphasia the sign functions are unreliable. The person with motor aphasia cannot give reliable signals. The patient with sensory aphasia has no clear insight concerning the word signals he receives. He may understand the emotional and general meaning of a signal, yet may miss the specific meaning of the word he hears. In this respect aphasia is a regression to a more primitive state in the signal function of language. In this primitive state the differentiation between foreground and background, or between figure (the term of gestalt psychology) and background, is not possible. In all cortical lesions of the brain not concerned with the more primitive motor and sensory functions, the relation between figure and background is disturbed. The background of experience has been given different names: the unconscious (Freud); fringes (James); the sphere (my term). The general plan of the organization of the brain seems to be that lesions of different localization disturb the relation between foreground and background. The localization of the lesion determines in which sphere of experience this basic disturbance appears. Motor aphasia and sensory aphasia are due to lesions of different areas of the cortex. This holds true also of agnosia and apraxia. Dr. Kennedy described a case in which the function of drawing was disturbed, owing to a localized lesion. In connection with well localized lesions of cortical areas, gnostic and practic functions also revert to a more primitive stage of function, in which the relation of foreground to background

is disturbed. One finds these disturbances in association with lesions of the posterior part of the brain. I believe in a rather exact localization in the cortical areas. The functions are, of course, not located in these specific areas of the brain, but without them the complete development of specific functions is not possible. This also holds true for apractic disturbances. I am convinced that Liepmann was right when he asserted that a lesion of the supramarginal gyrus produces apraxia. Agnostic and asymbolic disturbances can also occur in the course of localized lesions of the brain.

Since patients with aphasia usually behave correctly in simple surroundings, I am completely in agreement with Dr. Kennedy when he states that aphasic disturbance is not the same as disturbance of intellect such as is found in persons with dementia paralytica, arteriosclerosis and other diffuse lesions of the brain. For a finer differentiation of one's attitude to objects, however, abstract thinking is indispensable. For successful abstract thinking complete command of words and sentences is necessary.

Patients with aphasia show difficulties in the thought processes for which words are necessary. They have no longer free choice between abstract and concrete thinking, and their solutions are restricted to simple and concrete situations.

Persons with aphasia have "intellectual" disturbances. As already mentioned, these are different from intellectual disturbances in association with diffuse lesions of the brain. One should make oneself as independent as possible of the old terminology, which has lost its meaning in many respects. Instead of saying that the person with aphasia suffers from impairment of intelligence, one should say that he is in many instances unable to make social adaptation. He has emotional disturbances and disturbances in thinking. In the sphere of intellect and speech he differentiates incompletely between foreground and background. Since he cannot use signals freely, abstract thinking is difficult for him. If some one were to insist on the definition of the intellectual defect, one must state that the patient with aphasia has an intellectual defect which is different from the intellectual disturbances associated with diffuse lesions of the brain. He is not merely disturbed in speech and in the signal function but he is a different human being.

DR. ISRAEL S. WECHSLER: A point made by Dr. Kennedy which struck me with particular force is the tendency, which has become current in recent years, to speak psychiatrically in terms of systems. It is generally agreed that the retardation of medicine lay in the making of systems. Neurology, too, began to grow when systems of medicine ceased to exist, when persons began to be satisfied with small additions to knowledge. I refer now to the type of thinking which has given rise to such a term as total personality. It seems to me that it is one of the most meaningless concepts that has crept into psychiatric thinking. As one who is not altogether ignorant of psychiatry, though a neurologist, I believe that psychiatry is hurt by such concepts. They retard rather than advance knowledge. Instead of coming to grips with simple facts and trying to understand particular processes first and generalizing afterward, attempt is made to revert to former methods of thinking and to use general concepts, which merely act as a cloak for ignorance. Because of its vagueness, the term total personality confuses rather than clarifies thinking. Language may conceal as well as express thought, but it does not have to confuse it. The sooner such concepts are discarded the better it will be for psychiatry.

DR. FOSTER KENNEDY: I am enormously obliged to Dr. Tilney for his gracious remarks and for the aptness of his illustration of the poems of Homer. All ought to be grateful to Dr. Tilney for speaking of his personal experience. He would not like, perhaps, to say that his mind was intact while he could not speak for a time, so I will say that for him. He has assured me in private that he knew his mind was intact. To have the word of a good observer who knows objectively the signs of aphasia and has been able to view them subjectively is a great asset to scientific knowledge.

Dr. Henry spoke of the dualism of intellect and mind. Dualism, I think, has chained thought for two thousand years—the idea that the mind or the soul is something apart from the body and only loosely connected with it. I stated at the

beginning of the paper: "We regard mind, intellect, soul—whatever word you may use—as having the same relation to the body that sight has to the eye." If mind is viewed by itself one dwells among the mysteries, just as one deals with visual esthetics if one regards vision with no reference to the organ of sight.

Of course one must not confuse what today is called the total personality with the concept to which I objected, i. e., that of the total brain. I presume that if there is any meaning at all in the term total personality (and Dr. Wechsler has expressed a certain doubt) it is the ability of that personality to do one thing at a time. That is, I think, the purpose of the brain. As Dr. Wolf and I stated in our paper, that is what the brain tries to do through integration. It succeeds in obtaining a resultant of forces. I agree with Dr. Wechsler in his objection to the prevalent loose, mystic speech, the meaning of which the users do not carefully investigate. Total personality has yet to be defined. The speaker must say what he means if he is to be understood; the thought can be put into words. We believe as Dr. Wechsler stated, that from the building up of carefully considered facts the total fact will be found, the ultimate of which will always be elusive. The total fact is never to be discovered; only an adumbration of completeness can ever be reached; one must remember that the best motto for any man in medicine is *ex pede Herculem*. If one knows the foot of Hercules one can know Hercules, even if one does not see him.

NEW YORK NEUROLOGICAL SOCIETY AND NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

Joint Meeting, Jan. 14, 1936

LEON H. CORNWALL, M.D., *Chairman of the Section, Presiding*

ACTINOMYCOSIS OF THE CENTRAL NERVOUS SYSTEM: REPORT OF A CASE AND REVIEW OF THE LITERATURE. DR. E. D. FRIEDMAN, DR. ALFRED PLAUT (by invitation) and DR. HAROLD H. LEVY (by invitation).

On Feb. 20, 1935, A.B., a housewife aged 42, was admitted to the neuropsychiatric service of the Beth Israel Hospital with the chief complaints of chills, fever, headache and vomiting, of seven weeks' duration. The patient was of Italian descent but had been in the United States for forty years. She had been married twenty years and had four children living and well. Her past medical history was without significance except for two attacks of peritonsillar abscess. There was no history of colds, cough or expectoration or of disease of the skin or bones.

About seven weeks prior to her admission to the hospital she began to suffer from severe and persistent headache. The onset of the headache was followed by chilly sensations, fever (about 101 F.) and vomiting, which persisted for two days. She was confined to bed for ten days; after remission of all symptoms she attended to household duties. For a while she felt fairly well and made no complaint. The symptoms returned, and on Feb. 3, 1935, she was admitted to a hospital in Pennsylvania. There she had diplopia and ptosis of the left upper eyelid; vomiting ceased, but headache was severe and almost constant. She later suffered from mild sore throat. The condition, however, remained relatively unchanged until her admission to the Beth Israel Hospital.

Examination.—The patient appeared acutely ill but was alert and cooperative. There was no dyspnea, cyanosis or icterus. The skin was dark but presented no rash, petechiae or abnormality of pigmentation. The head was of normal size and contour; there were no evidences of injury. The ears showed no discharge, but the luster of the left drum was slightly dull. The mouth and buccal mucous membranes were normal. There was moderate congestion of the pharynx. The heart and lungs were normal. The abdomen and extremities showed no abnormalities.

Neurologic Examination.—The pupils were slightly irregular and reacted sluggishly to light; the right pupil was larger than the left. The optic disks were hyperemic with some obscuration of the margin, particularly on the right. There was moderate turgidity of the retinal veins. There were questionable weakness of the right external rectus muscle, more pronounced weakness of the left external rectus muscle and paralysis of the extrinsic muscles supplied by the left oculomotor nerve. The motor and sensory divisions of the fifth nerve were intact. The patient was aphonic. The uvula and entire posterior portion of the pharyngeal wall deviated upward and to the right on voluntary innervation. The left sternocleidomastoid muscle was paretic. The tongue deviated toward the left, and its left edge was furrowed. There was no paralysis of the extremities. The deep reflexes were present and equal on the two sides. The abdominal reflexes were not elicited. The plantar reflexes were slightly extensor in type. There was moderate nuchal rigidity with a Kernig sign. No sensory changes were elicited.

Course.—By lumbar puncture 25 cc. of thick, purulent fluid was obtained. Twenty cubic centimeters of antimeningococcus serum was given intrathecally, pending identification of the causative organism. The fluid was under a pressure of 320 mm. of water and contained 5,000 cells, 96 per cent of which were polymorphonuclear. The amounts of albumin and globulin were enormously increased, and there was no sugar. The Wassermann reactions of the spinal fluid and blood were negative. Examination of a smear of the fluid revealed no organisms, and culture proved sterile. Blood examination revealed 4,890,000 erythrocytes, 98 per cent hemoglobin and 16,200 leukocytes, with 85 per cent polymorphonuclear cells. The urine was normal. Lumbar puncture was again performed on the next day, and 50 cc. of spinal fluid was removed. On this occasion there were 29,300 cells per cubic millimeter, with a large percentage of polymorphonuclear leukocytes. No organisms were observed.

On the third day the patient appeared more comfortable. The only change in the neural status was diminution of the signs of involvement of the third nerve on the left. She felt much improved. Intravenous infusion of 500 cc. of hypotonic saline solution was given, followed by spinal drainage. Thick, green purulent fluid was obtained, which coagulated spontaneously after a few minutes. The laboratory of the New York City Board of Health reported large numbers of polymorphonuclear cells and enormous numbers of gram-negative organisms which were believed to be Bacillus influenzae.

On the fourth day the general condition of the patient remained fairly good. The manifestations of ocular palsy were still definitely less pronounced, and the entire course seemed slightly less ominous. Because of the viscidity of the spinal fluid and the difficulty with which it was obtained by lumbar puncture, it was decided to attempt simultaneous cisternal and lumbar punctures, with injection of physiologic solution of sodium chloride into the cisterna. However, only a few drops of extremely thick fluid was obtained by the lumbar puncture, and 60 cc. of similar fluid was removed from the cisterna. This fluid was not examined for cells because it coagulated immediately. Examination of the smear revealed nothing significant.

Throughout her stay in the hospital the patient's temperature fluctuated between 99 and 102 F. On the fifth day the temperature suddenly rose to 105 F. There appeared to be no other change in the condition; the pulse and respiration were unaltered, and the patient appeared as comfortable as before. However, with no further premonitory sign she suddenly ceased breathing.

Postmortem Examination.—The observations were not significant except in the central nervous system and the skull.

Spinal Cord: The outer surface of the dura was hyperemic in its entire length. During removal of the vertebral laminae, light yellowish green, thick pus oozed into the spinal canal from beneath the dura; this occurred chiefly in the lumbar and cervical regions.

Brain: The cranial bones were heavy, with little diploe. The soft meninges at the convexity and notably along the larger fissures were slightly dull and

thickened. No pus or fibrin was seen on the convexity. As the brain was removed, a large amount of thin, turbid, yellowish gray fluid escaped from the foramen magnum. The central portion of the spaces at the base of the brain and the cisterna pontis cisterna and magna were filled with thick, purulent, greenish yellow material. Large amounts of yellowish pus were obtained from the left cavernous sinus. The hypophysis appeared large and was shelled out with unusual ease. The surrounding tissues appeared soft. The left middle ear contained thin, bloody fluid. The sphenoid sinus contained mucopurulent material.

The hypophysis and surrounding tissue were bisected after fixation in a solution of formaldehyde. The capsule was distinct throughout. At one pole about one third of the anterior lobe appeared to bulge, and the usual markings were lost. The anterior lobe contained four small irregular cavities, which contained brownish material.

Microscopically the purulent tissue from the left pole of the hypophysis contained a large mycelial mass, which was obviously one of streptothrix. No clubs were present. The entire hypophysis was surrounded by thick, inflammatory layers in which mononuclear plasma cells prevailed. These cells were observed also in the immediate vicinity of the fungus granules. Smaller fungus granules were seen in other parts of the meninges. In the anterior lobe of the hypophysis several rather large irregular areas were seen in which the epithelial structures were supplanted by fibrous trabeculae containing blood vessels and cells with large nuclei. The meningitic inflammation penetrated little into the brain tissue. A medium-sized mycotic granule was observed in the thick exudate over the lumbar region of the cord.

Comment.—Actinomycotic invasion of the central nervous system is extremely rare. The literature, however, contains a number of reports of proved cases of involvement of the central nervous system by pathogenic organisms belonging to this group of higher bacteria.

The descriptions of the organisms have been so meager that no satisfactory classification has been made. They have been variously described as Streptothrix and Actinomyces. We have examined such reports of cases as we have been able to find, particularly from the point of view of the portal of entry, method of dissemination and type of pathologic involvement, and have endeavored to find characteristics which might be typical of this unusual neurologic condition. The pathologic picture is complicated by the fact that in many cases the nerve involvement was secondary to foci elsewhere in the body or to infection with other organisms.

Actinomycotic infection of the central nervous system does not produce a distinct clinical entity. The two types of pathologic changes (abscess and meningitis) differ widely in their clinical representations; the course of the disease is naturally modified more by the type of pathologic change and by its location in the central nervous system than by the nature of the causative bacteria. Furthermore, in the great majority of cases involvement of the central nervous system is secondary and the neurolgoic manifestations may be only part of the entire picture. However, a review of cases reported revealed a few characteristics which occur in a sufficiently large percentage of instances and which are not usual in association with abscess or meningitis caused by the more common organisms. We refer particularly to the frequency of spontaneous remission, the extreme purulence of the spinal fluid, the comparative well-being of the patient until shortly before death and the tendency of the disease to involve the perihypophysial region. All these characteristics were well illustrated in our case.

Age and Sex: The condition has been reported in patients of all ages, but we found, as Howard reported, that "it has a tendency to occur in males in the prime of life." Males are much more commonly affected than females. In infants and young children abscess occurs far less frequently than meningitis.

Geographic Distribution: Cases have been reported from all over the world. The disease is more common in rural districts, paralleling the occurrence of the more usual types of actinomycosis.

Method of Invasion: Many observers question the existence of primary infection of the central nervous system with Streptothrix and insist that a primary

focus, possibly healed or overlooked, existed elsewhere in the body. In 23 of the 107 cases of which we collected reports, the involvement was described as primary, but in examining the reports of autopsy we found that in many instances there was no record of examination of the sinuses, middle ear and other parts which may have originally harbored the organism. It is probable that lesions in such localities, either healed or overlooked, may have accounted for involvement in many cases of so-called primary infection.

In cases of cerebral actinomycosis in which a primary lesion is demonstrable, the question arises as to the route by which the central nervous system is reached. These paths are two: direct extension and metastasis. Evidence of direct extension was observed in 22 cases and of extension from the bones of the jaw in 7, from the middle ear in 6, from the temporal region in 2, from the face in 2 and from the pharyngeal tonsil, gums, buccal mucous membrane, sphenoid sinus and esophagus in 1 case each. In the last instance extension occurred to the vertebrae and spinal cord.

Since actinomycosis is essentially a disease of the connective tissue, direct extension occurs rather slowly through the bones of the skull. More commonly the extension is through the connective tissue surrounding the vessels and nerves which traverse the bone.

There is experimental, pathologic and clinical evidence to prove that metastasis does not occur through the lymphatics. This disease rarely if ever attacks the lymphatic structures, and adenitis when present is due to secondary infection. Although the lesions of actinomycosis usually spare blood vessels, there is no doubt that in the majority of instances metastatic lesions occur through the blood stream. In 20 cases the lungs and bronchial glands served as the source from which hematogenous infection of the brain occurred. In 14 cases there was generalized septicemia, the central nervous system being incidentally involved with the lungs, liver, kidneys and spleen. In many other cases primary lesions in the skin, ribs and other bones metastasized to the lungs and caused lesions which in turn acted as foci for hematogenous spread to the nervous system.

Pathologic Changes: These may be of two types: (1) localized, such as abscess or neoplasm, and (2) diffuse, such as meningitis.

In 34 cases meningitis occurred alone, and in 9 instances it was accompanied by abscess. In cases of meningitis the exudate is extremely purulent and almost invariably is confined to the base of the brain. Meningitis of the convexity is rare. The region around the hypophysis and the hypophysis itself are often bathed in the extremely thick, viscid, yellowish or yellowish green pus which is characteristic of actinomycotic meningitis.

The abscess may be large or small, single or multiple (more often single) and may occur in any part of the brain. However, the sites of predilection are the motor cortex, the centrum ovale and the region bordering on the third ventricle; the hypophysis is involved in a surprisingly large number of cases. The cerebellum is usually spared.

Lesions involving the walls of the ventricles or occurring in the ventricles themselves differ usually from abscess of the ordinary type. These lesions consist of soft cystic masses surrounded by a fibrous capsule, and grossly they may resemble a myxoma. When incised they are observed to contain a gelatinous substance resembling that in a cystadenoma of the ovary. This material differs from the pus in other types of abscess caused by Streptothrix and contains mainly albumin, mucin and degenerated lymphoid cells.

Spinal Fluid: The spinal fluid in the cases of meningitis is characteristic. It is extremely thick and purulent and contains enormous amounts of protein. The fluid is often obtained with difficulty by lumbar or cisternal puncture and may coagulate spontaneously. When actinomycotic meningitis complicates meningitis of other types, as occurred in a small epidemic described by Sindoni, the onset of the complication is accompanied by marked increase in the purulence of the spinal fluid.

Course and Symptoms: The two types of pathologic change cause a marked variation in the clinical course. Furthermore, the location of the lesion, as in most neurologic conditions, is the important determinant in the clinical picture.

Headache, vomiting, ocular symptoms, papilledema, vertigo, convulsions, paralysis and other symptoms which are usual in association with meningitis or abscess of the brain are common. Delirium and coma are frequent. The most remarkable and consistent clinical finding is the absence of toxicity and the apparent well-being of the patient, as well as the spontaneous, complete or nearly complete remissions which occur in the course of the disease. A patient who is paralyzed, delirious or comatose may, for no apparent reason, suddenly improve to a remarkable extent, only to suffer a relapse in one or two days, with progression of the previously existing symptoms. Several remissions may occur in the course of the illness.

Treatment and Prognosis: Unfortunately, little can be said as to therapy in this condition. Treatment remains symptomatic. The disease is invariably fatal.

DISCUSSION

Dr. Alfred Plaut: I will show a few representative slides from material in the case Dr. Levy described.

Actinomycotic infection is more frequent than the clinical diagnosis is of this condition. In our case the granules were observed accidentally; if we had not been in the habit of removing the hypophysis at autopsy, we should have overlooked the actinomycotic character of this condition. The diagnosis of actinomycosis generally is made only when one suspects the disease in the examination of the gross specimen. The surgeon who is familiar with the entire clinical course in his case is in a better position than the pathologist to think of the possibility of actinomycosis. When one observes unusually thick pus one should think of actinomycosis. By spreading the pus in a thin layer on a dark background one will see the characteristic sulfur-yellow granules with the naked eye. When surgeons consider the possibility of actinomycosis and search for sulfur granules, the percentage of cases in which actinomycotic infection is recognized is increased. On the other hand, not in all instances does infection with this organism bring about the formation of the actinomycotic granule. Infection with Streptothrix can be recognized only by applying suitable staining methods, notably the method of Gram, to sections of the diseased organs. In some cases the streptotrichal infection runs a septic course.

The interesting question whether or not the actinomycotic meningitis originated in actinomycotic infection of one of the accessory nasal sinuses cannot be answered in this case, for at the time when the character of the meningitis was recognized no material from the nasal sinuses was available.

Sometimes a lesion in the jaw, the lung or an abdominal organ suggests actinomycosis, but no granules are observed on the usual examination. In our experience, extensive search of many organs has led in several instances to detection of the actinomycotic granule.

Dr. Josephine B. Neal (by invitation): Dr. Levy mentioned that a specimen of spinal fluid from this patient was sent to the laboratory of the New York City Board of Health. My associates and I should have been able to report correctly on the cultural examination of this fluid. Unfortunately, the specimen came at a time when the laboratory was being moved, and owing to trouble with the incubator and other factors, we were not able to keep the cultures under observation for two weeks or more, as we usually do. We make a diagnosis of actinomycosis or streptotrichal infection only when we secure a culture containing the branching forms, and this often takes several days. I am sure that in times past, before we had as careful bacteriologic work as we have now, we missed instances of this infection. I remember a patient whom I saw many years ago a smear of whose spinal fluid suggested a mixed infection with the influenza bacillus and a gram-positive coccus. We relied mainly on aerobic cultures at the time and were surprised that in spite of the large number of organisms in the smear we were never able to culture them. In the spinal fluid the actinomyces are usually gram amphophilic; specimens stained by the Gram method often show a gram-negative bacillus and a gram-positive coccus, suggesting a mixed infection. It is not often that one sees the branching forms in the direct smear. Usually

we have been able to demonstrate the growth of the organism only in anaerobic culture. In one or two instances the cultures have grown aerobically.

We have seen and made the diagnosis in only 8 cases of meningitis due to actinomycosis. In all these cases diagnosis was made by means of cultures of the spinal fluid or, in 1 instance, by ventricular puncture performed after death. The patients ranged in age from 11 months to 46 years. All except 1 was less than 20 years of age, and 7 of the 8 were males. It was not possible to have a necropsy performed in most cases, hence in many instances correlation with the primary focus of infection could not be made. In 1 case the disease developed during convalescence from meningococcic meningitis; in another it followed extraction of infected teeth, and the observations at necropsy suggested that the alveolar abscess was the original focus of infection. In another case there was an abscess in the sphenoid and lateral sinuses, extending into the transverse sinus, but the pus was not cultured at the hospital where the autopsy was made; so we could be sure of the focus of infection.

The course of the illness in most of the cases was extremely short. Occasionally there was a history of severe headache for a longer time, but after the acute illness began the course was usually not more than four or five days, except in 2 instances. In 1 case, that of infection following meningococcic meningitis, the duration was about a month. In the case in which meningitis followed removal of an infected tooth the duration of illness was two months.

The most striking symptoms in most of our cases were the overactive deep reflexes and a much greater degree of spasticity than is characteristic of patients with meningitis due to the more common micro-organisms.

VENTRICULOGRAPHY WITH THE USE OF COLLOIDAL THORIUM DI-OXIDE. DR. WALTER FREEMAN (by invitation).

Colloidal thorium di-oxide mixes freely with the ventricular fluid and, because of its high specific gravity, sinks into the dependent portions of the ventricular system, making it possible to visualize the preoptic recess, the infundibulum, the aqueduct and the fourth ventricle, as well as the hooklike terminal recess of the temporal horn. Since thorium di-oxide is highly opaque to roentgen rays, relatively small quantities are required for satisfactory visualization of the whole system. When there is no obstruction to the ventricular outlets the material is rapidly eliminated, so that in as short a time as two hours no further shadow of the ventricles is obtained. Thorium di-oxide collects in the reticulo-endothelial system, particularly that of the liver and spleen, although in the amounts used for ventriculography no shadow of these organs is observed (Freeman, W.; Schoenfeld, H. H., and Moore, C.: Ventriculography with Colloidal Thorium Dioxide, *J. A. M. A.* **106**:96 [Jan. 11] 1936).

It is my purpose in this paper to discuss, first, the fate of the material when the outlet of the ventricles is obstructed, with its effect on the choroid plexus, ependyma, meninges and cerebral substance; second, the general diagnostic value of the ventriculograms obtained with this method, and, third, the possibilities of the use of colloidal thorium di-oxide in the visualization of intracerebral cyst and in the estimation of the extent and maturity of abscess cavities.

Fate of the Injected Medium: In cases in which there is no obstruction to the ventricular system, thorium di-oxide is rapidly eliminated, being carried over the surface of the cerebrum and passing through the arachnoid villi into the venous sinuses. Only microscopic amounts pass down the spinal canal or remain in the meninges. It is said that the perineural lymphatics may be visualized after injection of the material into the cistern, but my associates and I have had no experience with this. In cases in which the normal current is partially or completely obstructed, the protective colloid is dispersed, and the particles of thorium aggregate, forming clumps and sheets that adhere to the ependymal surface, or more probably to the subependymal tissue, for there is evidence that the ependyma is desquamated under the irritative influence of the retained material. The clumps of thorium di-oxide decrease in size from day to day but remain in situ

for a prolonged period. Up to the present there is no definite indication that the clumps of aggregated thorium di-oxide with the surrounding inflammatory reaction may cause obstruction at a critical point. In a case in which the patient was under observation for eleven days the fourth ventricle was not visualized in the early films but appeared as moderately dilated and sharply outlined at the end of this period. Evidently, there was considerable accumulation of the material in the walls of the fourth ventricle.

The earliest reaction appears to be in the choroid plexus. An hour after the injection, when there is as yet no alteration in the ependyma, leukocytes are observed over the surface and in the meshes of the choroid plexus. Within twenty-four hours, even in cases in which there is ventricular obstruction, the choroid plexus appears practically normal. At first there is no change in the ependyma, but within twenty-four hours there is a tendency to desquamation, with a minimal reaction on the denuded surface. Small granules are seen adhering to the surface after twenty-four hours, and in four days there are definite inflammatory foci, appearing as minute hemorrhagic spots in the gross specimen and as focal areas of inflammatory infiltration under the microscope. It may be said in passing that our only opportunities for pathologic examination have come in cases in which ventricular obstruction was presented. At the end of four days leukocytes are no longer present, but numerous phagocytic histiocytes are loaded with granules of thorium. We believe that these cells are derived not from the ependyma but from the blood stream by way of the choroid plexus, since they can be seen in considerable numbers both within and on the surface of the choroid plexus at the expiration of twenty-four hours, when the ependyma is as yet only mildly edematous.

With the passage of time, up to two months, these small nodules, consisting mostly of histiocytes filled with thorium granules, are incorporated into the wall of the ventricle, permeated by glial fibrils and effectively buried. The reaction extends little beneath the ventricular surface, and there is no indication of inflammation of a productive granulomatous type which conceivably might cause trouble later. Indeed, other investigators have shown that there is gradual dispersion of the thorium granules, which may be observed even in the cytoplasm of glia and ganglion cells.

The reaction in the meninges is relatively transitory. During the first two days moderate numbers of leukocytes may be observed; then, according to Lange, eosinophils make their appearance, but almost from the beginning the field is dominated by histiocytes. There is slight stimulation of the fibroblasts, and in the fissures at the base definite thickening of the meninges is present. At all stages, however, even months after the injection, granules of free thorium di-oxide may be observed, indicating that the material is so inert that it does not stimulate complete phagocytosis.

General Diagnostic Value: Films obtained after the injection of colloidal thorium di-oxide into the ventricles are striking, owing to the complete filling of the ventricular system. It is probable, however, that a set of normal pictures will have to be elaborated in order to interpret the films exactly. The mottled filling defect of the choroid plexus is revealed in many instances, as well as the serrated outline of the third ventricle. A peculiar appearance suggesting laceration of the anterior horns of the lateral ventricles was observed in a case of suspected cerebellar tumor. A definite filling defect in the region of the foramen of Monro was disclosed in 1 case; on account of the symptoms this patient was submitted to a cerebellar exposure, with no abnormal findings but thus far with apparent recovery. Of considerable importance is the diagnosis of block at the foramen of Monro. In 2 cases this was easily visualized, and in both instances fatality resulted, in 1 within an hour and in the other within twenty-four hours. We are inclined to attribute death in these instances to complications in intracranial pressure, since in each case it was impossible to find the opposite ventricle and the patient died before the maximum irritative effects of colloidal thorium could be expected. It is particularly in the diagnosis of tumors of the third and

fourth ventricles that the method has great possibilities, since in these conditions there is likely to be no shift of the ventricles and since it is difficult to fill these portions of the ventricular system with air. Our experience in this field is still too limited, however, to speak with decisiveness. On the whole, we prefer the use of this material to that of air both on account of the better cooperation given by the patient and because of the increased definition of the picture, and we are inclined to employ colloidal thorium di-oxide in any case in which there is probability of tumor, without definite localizing signs.

Cyst and Abscess: Immediately after the injection of colloidal thorium di-oxide into the cavity of a glioma there results a more or less opaque shadow on the films. After a day or two, however, the wall of the cyst stands out with startling clarity, owing to fixation of the thorium in the walls of the cyst in a manner analogous to that which takes place in obstruction of the ventricles. A sharp, balloon-like outline results, which indicates immediately the depth and extent of the cyst and may even disclose the mural nodule.

In only 1 case in our series was colloidal thorium di-oxide injected into the cavity of an abscess, but we believe that the method may be of value in determining not only the extent of the abscess but its encapsulation. As in other cavities, the thorium is fixed in the wall after a time. If the wall is clearly outlined it is probable that the abscess is encapsulated, whereas if the outline is blurred the abscess is almost certainly not encapsulated. In the case studied by Dr. Schoenfeld, in which, unfortunately, no pathologic specimen was obtained, the roentgenogram revealed the outline to be sharp in one sector and indefinite in other sectors. The future will tell whether this method is a practical means of deciding when operation will be most successful. We believe that with due care in the avoidance of contamination of the overlying meninges it will be possible to make this examination, but whether it will also reveal evidence of multilocularity of the abscess can only be guessed.

In delineating an area of infarction colloidal thorium di-oxide has been used by Radovici and Meller by cisternal injection. In their case the material apparently was phagocytosed by histiocytes in the infarcted area and was revealed as a definite shadow in the roentgenogram taken several months later, after removal of the brain.

DISCUSSION

Dr. H. H. Schoenfeld (by invitation): My colleagues and I carried out the first ventriculography with thorium in August 1933. We believe that the indications for the use of this technic are those which are commonly held as proper for ventriculography with air. We have attempted to inject the material by the spinal route in only 1 case, and in this instance we did not obtain satisfactory pictures of the cerebral fluid space. In the use of air in the ventricles, patients must be placed in such a position that the placing of the intraventricular needle permits the air to rise and the fluid to fall. That requires special equipment and also entails technical difficulties at times. By the use of this opaque material we find that we are not particularly interested in the position of the patient, except as concerns his comfort, and we are free to make the surgical approach and the needling of the lateral ventricles without regard to position. We gently mix the thorium with the cerebrospinal fluid back and forth in the syringe several times. Unless there is block, we can be certain that the thorium will be distributed well throughout the cerebrospinal fluid.

From the standpoint of the roentgenologist, we have simplified the technic of making good films. Air rises; fluid falls. There may be pocketing instead of a homogeneous mixture. To make films with air a swiveled Bucky diaphragm is required and swiveled tubes are needed for exposure of films from below upward if the best results are to be obtained. With the opaque material the usual, everyday roentgen equipment can be used satisfactorily, with good results.

The question of the patient's reaction is always raised. We have had one or two rather severe reactions, particularly in a patient with basilar meningitis. This child was acutely ill, with increase of all the meningeal signs, for about a

week after the injection. However, as roentgenologists claim, the majority of patients are much more comfortable than those for whom air is used. In a number of cases in which I used air first and thorium later, the patients stated definitely that they would allow the ventriculogram to be made again, but with thorium. The increase in temperature and pulse rate and the apparent illness are much less.

The question of the thorium remaining in cases in which there is block invites attention. Following a suggestion a few months ago by a neurosurgical colleague, we have advised that an indwelling cannula be placed in the ventricle after the making of the roentgenogram, so that the thorium may be washed out by the cerebrospinal fluid, and in at least 1 case the method has been practiced. This procedure has also a beneficial effect in decompressing the ventricular system, and I believe this will obviate any possible criticism that might be offered to the use of the foreign material in the ventricular system. Perhaps a somewhat better opaque material than thorium di-oxide may be found, but until then it is our conviction that the method is relatively safe, certainly as safe as injection with air. The advantages from the diagnostic standpoint are apparent.

DR. CHARLES WADSWORTH SCHWARTZ (by invitation): It has been evident to all neurologists for years that air is not the ideal medium to inject into a cavity that is normally filled with fluid, for air and water do not mix and frequently rather confusing shadows due to the formation of bubbles are obtained. This difficulty would be eliminated if one could find a material that is thoroughly miscible with the fluid. Many years ago my associates and I tried to find that material. We made roentgenograms of many test tubes filled with the halogen salts in various concentrations, in the hope of finding the desired medium; unfortunately, all these salts in sufficient concentration were too toxic. A few years ago we thought that the ideal substance might be found in the materials used for the intravenous production of pyelograms. We injected some of this material into the cistern of cats, but the cats died so quickly that we gave up that procedure. I believe that the ideal substance will eventually prove to be a true solution and not a colloidal suspension, for the colloidal suspension is always in danger of flocculating and becoming deposited, as Dr. Freeman has so well demonstrated in some of his slides.

Dr. Freeman raised the question of the radioactivity of thorium. I think one can disregard this factor, for thorium is not highly radioactive. Its half-life value is about thirteen billion years, whereas radium has a half-life value of one thousand six hundred and ninety years. As the radioactivity of a metal is in direct proportion to its half-decay period, one can see that thorium is almost inactive. In view of the fact that the brain can withstand tremendous doses of radiation without ill effects, it is evident that the extremely small amount from thorium would have no appreciable effect.

In Dr. Freeman's slides I noticed that the shadows of the basal structures were absent. We have come to consider the visualization of the basal cistern and the adjacent structures as being of considerable importance, and in many cases we base the diagnosis on small changes in the various cisterns. It is, however, possible for some thorium di-oxide to enter the basal cistern. I saw one case, in which thorium after injection passed not into the ventricle but apparently into the subarachnoid space, thus permitting visualization of some of the basal structures. I wonder what the reaction might be if thorium di-oxide were deposited in the walls of the basal cistern. If any swelling were produced it seems possible that some of the small complicated passageways might be obstructed. At the Neurological Institute we have had a reasonably large experience with injection of air, and by careful regulation of the amount of air introduced and by taking an adequate number of films with the patient in various positions we have been able to see practically all the pathways for cerebral fluid. This seems to preclude the necessity of using any other material than air to demonstrate these structures unless it was something that would cast a better shadow and had no added danger attached to its use.

There are, of course, many conditions in which ventriculography must be resorted to, such as tumor in the posterior fossa or nonneoplastic block of the aqueduct or the fourth ventricle. Unfortunately, in some of these cases, after puncture of the ventricle has been made little fluid can be obtained. In such cases a few cubic centimeters of thorium di-oxide might well be injected; this would undoubtedly give a better ventricular visualization than could be obtained with a few cubic centimeters of air. I wish to ask Dr. Freeman whether he has injected several cubic centimeters of thorium di-oxide into the lumbar region of the spinal canal and has followed its distribution for the next few hours. It seems to me that it might find its way out along some of the nerve sheaths, as iodized poppy-seed oil does when it is in the canal for a long time; using that method, one might have another and better way of visualizing the main nerve trunks.

Dr. Leo M. Davidoff: There is a question I wish to ask: While the opaque substance gives sharp, clear outlines of the ventricles, does not the very opacity of the shadow of the ventricles destroy some of the details obtained in outlining the ventricle with air? The air shadows are themselves translucent, so that one can look through the shadow of the ventricle as it is presented in the roentgenogram and can in this way outline many of the finer structures, whereas I should think that the opaque shadow would obstruct the view.

This method, as I see it, has many advantages over the use of air, but I believe it is limited to cases in which as Dr. Freeman said, ventriculography rather than encephalography is indicated. Therefore its use is relatively restricted, at least from the point of view of practicability at the Neurological Institute, where the series of encephalographies runs well into 3,000 and the number of ventriculographies is about 500.

A further point is the undesirable reactions which Dr. Freeman has described in cases in which there is likely to be obstruction of the ventricular system at any point. Since obstruction occurs most frequently in cases in which tumor of the brain is present, I wonder if that does not further limit the use of this method.

Dr. John E. Scarff: In any discussion of ventricular visualization account should be taken of gases other than air. In Montreal last spring I was much impressed with the work of Dr. Wilder Penfield and his associates in experimenting with other gases. Following their suggestions, my associates and I have been doing the same thing at the Bellevue and the New York Post-Graduate Hospital. We worked chiefly with oxygen and found that some objections to the use of air, which Dr. Freeman has overcome by means of his liquid medium, can be met by using oxygen instead of air. First, oxygen is far less irritating than air to the ependyma and the subarachnoid spaces. For example, recently I injected without the use of anesthesia 90 cc. of oxygen into the ventricles of a child aged 7, who asked not to be tied. It was not necessary to restrain the child, and she made no complaint during the injection of this gas. The second advantage of oxygen lies in the fact that it is absorbed in from one half to one third of the time required for air. This has considerable significance. The period of maximum pressure and therefore the period of danger after the injection of air into the ventricles occur in perhaps from one to three hours. Why the pressure should be greater at that time is not clear, but it may be due to two factors: irritation of the ependyma, which increases the secretion of fluid, and possibly tiny multiple emboli of air trapped in the arachnoid spaces, which retard the absorption of spinal fluid. On the other hand, from the moment oxygen is introduced, the intracranial pressure becomes less. So striking is this that it is necessary to inject at one time from a fourth to a third more gas than the volume of the fluid removed. For instance, for every 5 cc. of fluid removed we inject 7 or 8 cc. of gas. We have had opportunity to watch the intracranial pressure after injection of oxygen into the ventricles in persons who had undergone operation for decompression and found that within one-half hour or an hour the area of decompression was much softer than at the time when the gas was placed inside

the ventricle. It is now our usual practice to introduce 25 per cent more oxygen than the volume of the fluid removed. In cases in which encephalography has been made for the relief of jacksonian attacks in the absence of choked disk, it is our experience to have the patient walk about the ward within twenty-four or forty-eight hours after the test, without headache or other major complaint. This, of course, is in striking contrast to the situation after the use of air.

DR. CORNELIUS DYKE: May I ask Dr. Freeman why he stated that in one of the ventriculograms there was evidence of laceration of the frontal lobes?

DR. WALTER FREEMAN: We think that colloidal thorium di-oxide should not be injected into the cisterns. For one reason, practically all experimentalists believe that it is highly irritating in animals; second, there is a greater tendency to flocculation of the material when injected in bulk into the cistern than when injected into the ventricle. Such injections have been made by others; the material reaches the various cisterns and sometimes delineates them well, but, as Dr. Davidoff pointed out, they tend to overlap and obscure one another.

Dr. Schwartz is right in emphasizing the importance of the basal cistern. It is of definite importance in the diagnosis of certain lesions, and when there is a question of demonstrating it we prefer the injection of air by the spinal route. In one case I injected colloidal thorium di-oxide into the cistern, and in another, into the lumbar sac. In the first case the material was injected slowly and without mixing, in an unsuccessful effort to demonstrate pachymeningitis. After the injection into the caudal sac, we could observe the advance of the thorium shadow along the course of the sacral plexus. In work done in Germany, the thorium even appeared at the brim of the pelvis after several months.

Whether a true solution will be found that is satisfactory for this use is not certain. The ventricular fluid is so closely related to the original lymph that it is doubtful whether a substance excreted through the choroid plexus can be concentrated sufficiently to demonstrate the outline of the ventricles; we doubt whether any intravenous injection will give a picture of the ventricles. Whether a solution can be found which does not give rise to irritation on intraventricular injection is a question. I believe that the use of inert material like thorium di-oxide has many advantages, provided that it can be held in more stable suspension by a colloid. The irritative phenomena observed in the slides shown were due not to thorium but to the protective colloid dextrin, which is more or less diffusible and can be broken down.

I was glad to receive the confirmation of Dr. Schwartz that as a radioactive substance thorium is so inert.

Dr. Davidoff is correct in pointing out the danger of the use of this material in cases in which the ventricles are blocked. We believe that this objection may be obviated by draining the ventricles during a period of twenty-four hours or so after the injection, for during this period at least the thorium is held in suspension and is apparently not flocculated.

Dr. Scarff's comments are interesting but somewhat wide of the mark, for I have emphasized the difference between an opaque medium which is miscible in spinal fluid and a gaseous medium which is not. When any gas is used, unless the skill of the roentgenologist is adequate to the problem, there are bound to be pockets where the fluid will be caught, and the surgeon will frequently be misled by the appearance of the film. What we seek to do with this opaque colloidal medium is to bring about a satisfactory visualization of the whole system.

VISUALIZATION OF THE CEREBRAL VESSELS BY DIRECT INTRACAROTID INJECTION OF THORIUM DI-OXIDE. DR. JULIUS LOMAN and DR. ABRAHAM MYERSON (by invitation).

The technic of roentgenographic visualization of the cerebral vessels by injection of radiopaque substances into the carotid artery has been only sporadically adopted since its introduction by Egas Moniz, Pinto and Almeida Lima in 1931. The method described by these authors consists in exposing and ligating the com-

mon or the internal carotid artery, injecting colloidal thorium di-oxide and taking roentgenograms of the skull as the injection is completed. Since this method constitutes a major surgical technic, many surgeons have hesitated to use it. Because of this objection we have developed a more direct method of cerebral vasography, which may be learned after a short period. Briefly, the method is as follows: With the patient lying on his back, the side of the neck is sterilized and anesthetized with procaine hydrochloride; a needle attached to a syringe is inserted through the skin into the common carotid artery at the level of the cricoid cartilage. In order to make certain that the needle is well within the lumen of the vessel, the needle is connected by means of a stopcock to tubing and an aneroid manometer. If the puncture is successful, the manometer needle records wide oscillations, and compression of the carotid artery below the site of puncture causes a quick fall in pressure followed by a rapid return to the original pressure, with free oscillations when the compression is released.

If these conditions are met, the procedure is continued as follows: An assistant slows either the arterial flow to the brain by compressing the carotid artery below the site of puncture or, better still, the cerebral venous circulation by compressing both jugular veins. While compression of either type is continued, the operator injects as rapidly as possible 10 cc. of colloidal thorium di-oxide. Rapidity of injection and adequate compression of the neck until all the roentgenograms are taken are requisites for successful visualization of the cerebral vessels. Lateral plates are taken, exposure being a half-second. The first roentgenogram taken near the completion of the injection gives a beautiful outline of the internal carotid artery and its branches. A second and a third roentgenogram, taken at three second intervals, give good pictures of the cerebral veins and sinuses.

In 30 injections done by us neither immediate nor late ill effects have been observed. Not only may aneurysm of the internal carotid artery or its branches be directly visualized by this method but in many cases cerebral neoplasm may be indirectly located by the presence of dislocation of the cerebral arterial tree. It is probable also that other cerebral abnormalities may be determined by cerebral vasography.

DISCUSSION

DR. ISRAEL STRAUSS: Many neurologists have wished to make arterial injections of thorium di-oxide, but the objection to exposure of the carotid artery has always been encountered; most have been reluctant to subject the patient to what they believed was in many ways an unnecessary procedure, especially in cases in which it was suspected that the result would demonstrate an aneurysm in an inaccessible part of the skull. With this technic, however, I see no reason why one should not be able to utilize the method to advantage. It happens occasionally that a flat plate of the skull outlines the presence of an aneurysm by calcification of its walls. In other cases in which aneurysm is suspected one is sometimes forced to make an encephalogram to locate the pathologic process, but one is not certain whether it is aneurysm or tumor. In the case of aneurysm, particularly in the branches of the circle of Willis, the neurosurgeon is loath to operate because he is faced with an almost insuperable problem. He cannot remove the aneurysm in most instances. There are cases in which aneurysm can be diagnosed and located definitely in the posterior part of the interpeduncular space on the basis of the neurologic signs, but there again the surgeon is faced with great difficulty, for in that location the lesion is inaccessible. A small, superficially placed aneurysm occasionally occurs which may be demonstrated by injection of thorium di-oxide and successfully removed. In one case reported in which the aneurysm was not definitely localized, thorium di-oxide showed its position, and successful operation was performed. I think, therefore, that this method which is now available offers some promise of benefit in cases in which heretofore the condition has been beyond help.

DR. CORNELIUS DYKE: I wish to congratulate Dr. Loman and Dr. Myerson on devising a simple technic for puncturing the common carotid artery. This accomplishment removes one of the great deterrents to the use of arteriography.

Several questions come to mind. First, does Dr. Loman think there might be a more convenient method of retarding the venous blood flow from the intracranial cavity than the digital one? An apparatus was described by Cone and Grant (Graduated Jugular Compression in the Lumbar Manometric Test for Spinal Subarachnoid Block, ARCH. NEUROL. & PSYCHIAT. **32**:1194 [Dec.] 1934), who placed an ordinary blood pressure cuff around the patient's neck and pumped it up to the desired pressure. This could be maintained for an indefinite time. Such a method should make it easier to manipulate the patient during the taking of the films and, I believe, should more satisfactorily retard the flow of blood from the head.

The second question is: How much time has one in which to take the roentgenograms? I noticed that Dr. Loman showed only lateral views and that, if I am correct, they were taken without a Potter-Bucky diaphragm. From this it seems that only a few seconds are available for taking the roentgenograms. The value of the roentgenograms is greatly lessened if it is possible to obtain only a single lateral view, for one would be unable to determine a lateral displacement of the intracranial vessels. It might be worth while, therefore, to work out some method of taking an anteroposterior and a lateral view practically simultaneously.

Another point is that when injection is made into either common carotid artery the anterior and middle cerebral and the anterior communicating arteries are about the only vessels that are visualized. The procedure would, therefore, be of aid only in diagnosing a lesion in the anterior half of the intracranial cavity. Furthermore, an intraventricular tumor would not produce changes in the position of the vessels that would permit diagnosis. It seems to me that the principal use of this method, as Dr. Strauss has already remarked, is in making the diagnosis of vascular lesions, particularly aneurysm of the basilar vessels. It should be of special value in making a diagnosis of small sacculated aneurysms on which the surgeon can operate with success. My colleagues and I have had difficulty occasionally in making the differential diagnosis between pituitary adenoma and aneurysm of the internal carotid artery. The use of thorium di-oxide would clarify such a problem in a few minutes. Finally, it seems that the use of gas in encephalography and ventriculography is of considerably more value than that of thorium in the diagnosis of intracranial tumor.

DR. H. G. WOLFF: I wish to make some minor remarks on the velocity of the cerebrospinal blood flow. Some years ago Dr. Blumgart and I attempted to measure the speed of the blood flow in the head under normal conditions and during periods of increased intracranial pressure. We used cats for the experiments. A radioactive salt was injected into the internal carotid artery, and the time that elapsed from its injection to its reappearance in the right side of the heart was measured. When the necessary corrections were made we found that the speed of flow inside the head is, under conditions of average blood pressure, from three to six seconds. From three to six seconds after its injection the radioactive salt appeared in the internal jugular vein. I presume that Dr. Loman took a roentgenogram to illustrate the thorium in the veins about three seconds after the first picture showing it in the arteries. In injecting the thorium he slows the blood flow, but, nevertheless, it appears to take, as in the case of cats, about three seconds to pass through the human head. Is that your impression, Dr. Loman?

DR. WALTER FREEMAN: Neurologists who attended the Second International Neurological Congress in London may have seen some of the work of Egas Moniz, the pioneer in this type of cerebral photography. He first used iodide salts and found them too irritating; he shortly shifted to the employment of thorium di-oxide, which he injected by the open method in amounts as high as 18 cc. His time relationships were one and a half seconds for the arteries, three seconds for the capillary bed and four and one-half seconds for the veins. This corroborates some of the work reported here. He showed anomalies, distortion of the arteries, a few instances of hemangioma and, of course, disturbances in the outline of the veins. Some beautiful instances of intracranial aneurysm were presented, occasionally

bilateral. It seems to me that his work suffered from the fact that it necessitated surgical operation; if the contribution of Dr. Loman and Dr. Myerson is practicable the possibility of diagnosis of intracranial lesions by arteriography should be extended. I agree with Dr. Dyke that its use will be limited practically to vascular disturbances. There is, however, arterial dislocation due to tumor which is sometimes difficult to demonstrate; it may even be impossible of demonstration in the posterior fossa, because the arteries in the posterior fossa come from the vertebral and the basilar artery.

DR. RICHARD BRICKNER: Not much has been said of the risks involved in the procedure, and I wonder if Dr. Loman will discuss this aspect of the question. I wish also to ask him whether he thinks that the details of the vascular tree can be seen with sufficient refinement that the method may be used to study the state of the vascular system in such conditions as migraine. Could the hypothetic spasms in migraine be made visible by this method?

DR. JULIUS LOMAN: Dr. Dyke brings up several interesting points. Cerebral arteriography is still in its infancy. We were primarily concerned with developing a more simple technic than the open method heretofore used. We have thought of other methods of compressing the neck; Dr. Dyke's suggestion of using the blood pressure cuff around the neck is worth trying. All our plates thus far have been lateral exposures; we hope later to take anteroposterior plates. Dr. Dyke's suggestion of taking simultaneous roentgenograms is good and may be helpful in gaining more definite information about cerebral lesions. The posterior portion of the brain cannot be visualized by injection of the radioactive substance into the common carotid artery. There is a remarkable similarity of the cerebral arteries in all the plates if the technic is uniform, and although it may be true that the main use of the method will be limited to the diagnosis of aneurysm, I believe that in many cases tumor of the brain will be diagnosed by the dislocation of the cerebral arterial tree.

Dr. Wolff brought up the question of the cerebral blood flow. As he and Dr. Blumgart concluded, the cerebral circulation time of four seconds is probably accurate. The estimated circulation time by our method is about eight seconds. Of course, the blood flow is considerably slowed because of the necessary use of compression of the neck. Without the use of compression it is impossible to secure roentgenograms of the vessels, owing to the speed of the cerebral circulation and the resulting lack of concentration of thorium di-oxide in the brain. Adequate compression, either of the carotid artery or of the jugular veins, in addition to rapid injection of the opaque medium, are requisites to successful visualization of the cerebral vessels.

Dr. Brickner asked about the dangers or the method and the possibility of obtaining information concerning migraine by the use of cerebral arteriography. Thus far, we have made injections in 30 patients and have seen no immediate or late ill effect from the injections. In a few cases there was a slight rise in temperature after the injection. Many of the subjects utilized were of advanced years. Among the rest of the patients were persons with dementia praecox. I doubt that this method will prove useful in revealing the finer vascular changes such as may be present in migraine.

Book Reviews

The Carotid Sinus and the Cerebral Circulation: An Anatomical, Experimental and Clinical Investigation, Including Some Observations on Rete Mirabile Caroticum. By Erik Ask-Upmark. Price, 18 kroner. Pp. 374, with 72 illustrations. Copenhagen, Denmark: Levin & Munskgaard, 1935.

This voluminous monograph, published as the sixth supplement of the *Acta psychiatrica et neurologica,* is based on investigations which Ask-Upmark carried out in the departments of anatomy, neurology and neurosurgery of the Harvard University Medical School. The anatomic studies, with a thorough review of the literature, are valuable. The comparative anatomic features of the carotid sinus were studied in sixty-one animals, representing twenty-seven species of mammals, birds, reptiles and amphibia. The important point is made that the carotid sinus is always observed at the internal carotid artery if the artery is present. In species in which no carotid artery is present the sinus is located at the base of the occipital artery, indicating that the carotid sinus may play an important rôle in regulating cerebral circulation. Interesting data are supplied regarding the variations in the bifurcation of the carotid artery and developmental malformations. The rete mirabile caroticum is described in mammals. It is especially well developed in species in which the external carotid artery is the main channel for the cerebral blood supply and in which the internal carotid and the vertebral artery are insignificant or missing. On purely anatomic grounds a theory is presented that both the carotid sinus and the rete mirabile caroticum contain mechanisms which presumably protect cerebral circulation from sudden changes in pressure.

The results of the experimental studies indicate that the carotid sinus exerts an influence on cerebral circulation, manifested by visible changes in the pial arteries when the sinus is stimulated. The prevailing influence of the carotid sinus on cerebral circulation is that, as the structure is susceptible to alterations in systemic blood pressure, it warrants the continuity and the even level of blood flow to the brain. It is also suggested that the nerves supplying the carotid sinus may be of importance for the regular response of the cerebral vessels to vagal and sympathetic impulses.

In the clinical part of the book conditions are discussed in which the carotid sinus may be affected or in which it may contribute to the symptomatology. Syncope, epilepsy, cerebral vascular lesions, postural hypotension, glossopharyngeal neuralgia, tumor of the acoustic nerve in relation to the glossopharyngeal nerve, blood pressure associated with tumor of the brain, blood pressure during neurosurgical operation, and changes in the cardiovascular system following injury to the head are analyzed from the standpoint of the carotid sinus. A great deal of valuable information is accumulated in this section, but the tendency to develop the same thought contained in the discussion of the anatomic and experimental investigations makes the reasoning sometimes too forced and dogmatic.

The book is thought provoking, contains an excellent bibliography and is valuable to all workers interested in the mechanism of the carotid sinus and that of cerebral circulation. However, it is most suited to serve as a reference book, since, in spite of the vast amount of work, it does not materially advance knowledge of the subject. The English is somewhat difficult to read. Careful reediting and the avoidance of repetition would materially enhance its value.